

# RADIOLOGY

A MONTHLY JOURNAL DEVOTED TO CLINICAL RADIOLOGY AND ALLIED SCIENCES

Vol. 55

OCTOBER, 1950

No. 4

## CONTENTS

- SOME OBSERVATIONS WITH 1,000-Kv., 400-Kv., AND 200-Kv. X-RAY THERAPY. *Walter T. Murphy, M.D., and M.C. Reinhard, M.A.* 477
- RADIATION DOSIMETRY IN THE TREATMENT OF FUNCTIONAL THYROID CARCINOMA WITH  $I^{131}$ . *L. D. Marinelli, M.A., and Ruth F. Hill.* 494
- CEPHALOHEMATOMA IN THE NEWBORN.  
*M. D. Ingram, Jr., M.D., and W. M. Hamilton, M.D.* 503
- ROENTGEN DIAGNOSIS OF LIPOMA OF THE CORPUS CALLOSUM. REPORT OF A CASE.  
*Wylie H. Mullen, Jr., M.D., and John R. Hannan, M.D.* 508
- RADIOGRAPHIC CHANGES IN THE LUNGS DURING RECOVERY FROM DROWNING. *Jerome J. Romagosa, M.D. Leon J. Menville, M.D., and John T. Leckert, M.D.* 517
- TUBEROUS SCLEROSIS, A NEUROCUTANEOUS SYNDROME. REPORT OF A CASE.  
*Lt. Comdr. G. Charles Budenz (MC), U.S.N.* 522
- TRAUMATIC AND RELATED TYPES OF DIAPHRAGMATIC HERNIA.  
*Frank Isaac, M.D., Franklin B. Wilkins, M.D., and Jos. Weinberg, M.D.* 527
- SKELETAL METASTASES IN CARCINOMA. *Herbert L. Abrams, M.D.* 534
- DOUBLE-CONTRAST STUDIES OF THE COLON WITH SPECIAL REFERENCE TO PREPARATION AND FICTITIOUS POLYPS.  
*C. W. Yates, M.D., R. D. Moreton, M.D., and E. M. Cooper, M.D.* 539
- ROENTGENOGRAPHIC FINDINGS IN SCHÖNLEIN-HENOCH'S PURPURA. A CASE REPORT. *John S. Fetter, M.D., and William L. Mills, M.D.* 545
- SMALL INTESTINAL ABNORMALITIES IN ANAPHYLACTOID PURPURA. REPORT OF TWO CASES. *Joseph J. Esposito, M.D.* 548
- CORTICAL FISSURING IN OSTEOMYELITIS COMPLICATING SICKLE-CELL ANEMIA. *Russell Wigh, M.D., and Harvey J. Thompson, Jr., M.D.* 553
- EFFECTS OF INTERNAL IRRADIATION OF MICE WITH  $P^{32}$ . PART II. GONADS, KIDNEYS, ADRENAL GLANDS, DIGESTIVE TRACT, SPINAL CORD, LUNGS, AND LIVER. *Shields Warren, M.D., Jane C. MacMillan, M.D., and Frank J. Dixon, M.D.* 557
- DEPOSITION OF RADIOGALLIUM ( $Ga^{72}$ ) IN PROLIFERATING TISSUES.  
*H. C. Dudley, Ph.D., G. W. Imirie, Jr., B.S. and J. T. Istock.* 571
- RADIATION-INDUCED MUTATIONS IN MAMMALS. *Donald R. Charles, Ph.D.* 579
- TELOGNOSIS. *J. Gershon-Cohen, M.D., and A. G. Cooley.* 582
- CLINICAL CINEFLUOROGRAPHY.  
*Robert F. Rushmer, M.D., Raymond S. Bark, and John A. Hendron* 588
- EDITORIAL: THE NASOPHARYNGEAL APPLICATOR. *Harold W. Jacox, M.D.* 593
- PRELIMINARY SCIENTIFIC PROGRAM: THIRTY-SIXTH ANNUAL MEETING. 595
- ANNOUNCEMENTS AND BOOK REVIEWS. 598
- RADIOLOGICAL SOCIETIES: SECRETARIES AND MEETING DATES. 601
- ABSTRACTS OF CURRENT LITERATURE. 604

# RADIOLOGY

A MONTHLY PUBLICATION DEVOTED TO CLINICAL RADIOLOGY AND ALLIED SCIENCES

PUBLISHED BY THE RADIOLOGICAL SOCIETY OF NORTH AMERICA

## EDITOR

HOWARD P. DOUB, M.D.

Henry Ford Hospital, Detroit 2, Mich.

## ASSOCIATE EDITORS

John D. Camp, M.D.

Hugh F. Hare, M.D.

## PUBLICATION COMMITTEE

Harold W. Jacox, M.D., Chairman

Leo G. Rigler, M.D.

George L. Sackett, M.D.

## EDITORIAL ASSISTANTS

Marion B. Crowell, A.B.

Florence E. Roper, A.B.

## ADVISORY EDITORIAL BOARD

Harold Cummins, Ph.D.

Edith H. Quimby, Sc.D.

Arthur Purdy Stout, M.D.

## GENERAL INFORMATION

RADIOLOGY is entered as second class matter at Syracuse, New York, and Easton, Penna., under the Act of August 24, 1912, and accepted November 24, 1934. RADIOLOGY is published by the Radiological Society of North America as its official Journal. Subscription rate \$8.00 per annum. Canadian postage, \$1.00 additional. Foreign postage, \$2.00 additional. Single copies \$1.00 each. All correspondence relative to business matters connected with the Radiological Society of North America and RADIOLOGY, or remittance for non-member subscriptions, should be made payable to the Radiological Society of North America and should be addressed to the BUSINESS MANAGER, DONALD S. CHILDS, M.D., 713 E. GENESEE STREET, SYRACUSE 2, NEW YORK. In requesting change of address, both the old and the new address should be given.

Dues to the Radiological Society of North America include subscription to RADIOLOGY and should be paid to DONALD S. CHILDS, M.D., SECRETARY-TREASURER, 713 E. GENESEE STREET, SYRACUSE 2, N. Y.

The rate for "want" advertisements for insertion in the Classified Section is 8 cents per word, minimum charge \$2.00. Remittance should accompany order. Rates for display advertisements will be furnished upon request.

Inquiries regarding the program for the Annual Meeting of the Society for the current year should be sent to the President.

RADIOLOGY is published under the supervision of the Publication Committee of the Radiological Society of North America, which reserves the right to reject any material submitted for publication, including advertisements. No responsibility is accepted by the Committee or the Editor for the opinions expressed by the contributors, but the right is reserved to introduce such changes as may be necessary to make the contributions

conform to the editorial standards of RADIOLOGY. Correspondence relating to publication of papers should be addressed to the Editor, HOWARD P. DOUB, M.D., HENRY FORD HOSPITAL, DETROIT 2, MICHIGAN.

Original articles will be accepted only with the understanding that they are contributed solely to RADIOLOGY. Articles in foreign languages will be translated if they are acceptable. Manuscripts should be typewritten, double-spaced, with wide margins, on good paper, and the original, not a carbon copy, should be submitted. The author's full address should appear on the manuscript. It is advisable that a copy be retained for reference as manuscripts will not be returned.

Illustrations and tables should be kept within reasonable bounds, as the number which can be published without cost to the author is strictly limited. For excess figures and for illustrations in color, estimates will be furnished by the Editor. Photographic prints should be clear and distinct and on glossy paper. Drawings and charts should be in India ink on white or on blue-lined coordinate paper. Blueprints will not reproduce satisfactorily. All photographs and drawings should be numbered, the top should be indicated, and each should be accompanied by a legend with a corresponding number. Authors are requested to indicate on prints made from photomicrographs the different types of cells to which attention is directed, by drawing lines in India ink and writing in the margin. The lines will be reproduced, and the words will be set in type. Attention should be called to points which should be brought out in completed illustrations, by tracings and suitable texts. These instructions should be concise and clear.

As a convenience to contributors to RADIOLOGY who are unable to supply prints for their manuscripts, the Editor can arrange for intermediate prints from roentgenograms.

The Society will furnish fifty reprints to authors, for which arrangements must be made with the Editor.

Contents of RADIOLOGY copyrighted 1950 by The Radiological Society of North America, Inc.

# RADIOLOGY

A MONTHLY JOURNAL DEVOTED TO CLINICAL RADIOLOGY AND ALLIED SCIENCES

PUBLISHED BY THE RADIOLOGICAL SOCIETY OF NORTH AMERICA

Vol. 55

OCTOBER 1950

No. 4

## Some Observations with 1,000-Kv., 400-Kv., and 200-Kv. X-Ray Therapy<sup>1</sup>

WALTER T. MURPHY, M.D., and M. C. REINHARD, M.A.

Buffalo, N. Y.

THIS PAPER IS A report on several observations made during the course of routine treatment of malignant neoplasms by radiation of three different qualities, namely, 9.0, 5.0, and 0.9 mm. copper half-value layer. Experimental work which was carried on to clarify some of these observations is included. The following topics will be discussed:

- I. Total skin dose *vs.* treatment time relationship for the three qualities.
- II. Effect of increment and time spacing on skin and subcutaneous tissues.
- III. Comparison of reactions produced by equal doses of 1,000-kv. and 200-kv. radiation to the same patient.
- IV. Depth doses and reactions with radiation of the three qualities.
- V. End-results of treatment in carcinoma of the cervix with the three qualities.

A description of the general factors used in therapy at Roswell Park Memorial Institute for this study follows:

Voltage	1,000 kv.	400 kv.	200 kv.
Quality— h.v.l.	9.0 mm. Cu	5.0 mm. Cu	0.9 mm. Cu

Skin target distance	70 cm.	70 cm.	80 cm.
Dose rates	41.8	15.6	31.5 r/min. (air)

Henceforth all references to dosages delivered will be with tissue scattering, the values having been determined by ionization measurements made with a phantom at this Institute.

### I. TOTAL SKIN DOSE *VS.* TREATMENT TIME RELATIONSHIP FOR THREE QUALITIES

At the time of installation of the 400- and 1,000-kv. x-ray generators in 1940, there was a paucity of information available concerning tissue reactions with super-voltage. This fact made it necessary to rely on past experience gained from treatment with 200-kv. beams of x-ray and telecurie therapy and to proceed empirically with the x-ray treatment, in order to obtain some information on skin tolerances with voltages over 200 kv. Based on the information derived from the results of treatment of these early cases, the points shown in Figure 1 represent the total dose (incident plus exit) for one port as a function of the total number of days of treatment. The wide scatter of points is due in part to varying diameters of patients, in part to individual biological variation, and in part

<sup>1</sup> From Roswell Park Memorial Institute, Buffalo, N. Y. Accepted for publication in January 1950.

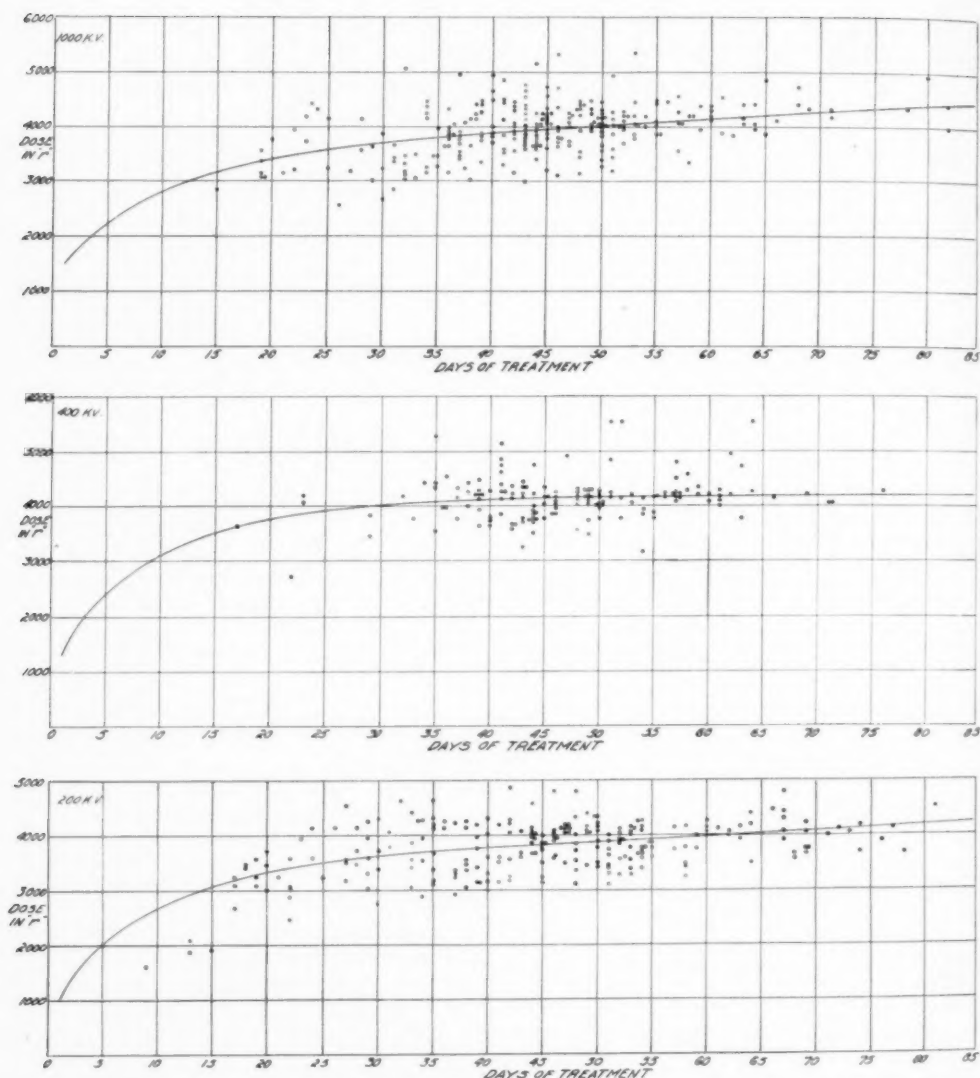


Fig. 1. Skin dose per port and time relationship in routine series of patients receiving pelvic irradiation.

to differences in the magnitude and time-spacing of the daily increments. It is to be emphasized that these are routine dosage values, not necessarily directed to produce equal skin reactions, although in most instances a so-called skin tolerance limit was reached, as evidenced by subsequent skin reactions.

Because of the scatter of points, the drawing of a representative accurate curve through them is difficult. The curves

shown in Figure 1 are free-hand curves drawn so as to bisect the points for the different time intervals as accurately as possible. It is evident from these curves, and from the distribution of the data, that for any treatment period there is no essential or significant difference in the skin dosage delivered by the three qualities of radiation. Routinely, patients given 1,000-kv. radiation received no greater skin dosage than those given 400 or 200 kv.

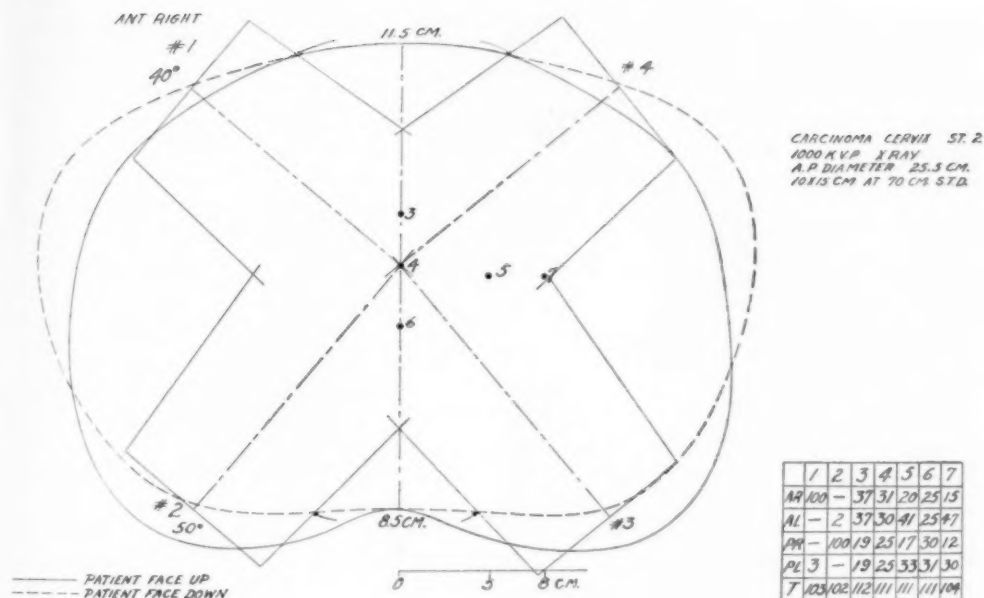


Fig. 2. Treatment technic diagram for four converging beams of radiation. Bolus placed in angle between skin and treatment cones.

## II. EFFECT OF INCREMENT AND TIME SPACING ON SKIN AND SUBCUTANEOUS TISSUES

One of the possible reasons for the scatter of the dosage values in Figure 1 is that a variety of combinations of increment magnitude and daily spacings were used. An experiment, therefore, was set up to investigate the influence of these two factors, as follows: Patients who were scheduled for a four-field radiation technic (for example, carcinoma of the cervix) were subdivided into two groups. The first

group received a small increment to each of four ports each day and the second group received an increment per port four times greater, but each port was treated once every four days. The over-all total treatment time was essentially the same for the two groups. Four converging beams of radiation were used, as shown in Figure 2. This program was carried out for all three qualities of radiation, as shown in Table I. All the skin reactions on the last day of treatment were essentially similar

TABLE I: VARIATIONS IN SKIN INCREMENTS, TIME SPACING, AND TOTAL SKIN INCIDENT DOSES PER PORT IN CONVERGING CROSS-FIRE PELVIC IRRADIATION

Four Ports per Day				
	Increment Dose	Cycles	Total Incident Dose per Port	Treatment Period in Days*
1.	100 r	40	4000 r	46-54
2.	125 r	32-35	4000 r-4375 r	37-47
3.	150 r	27-30	4050 r-4500 r	31-40
4.	175 r	23-25	4025 r-4375 r	31-35
One of Four Ports per Day				
5.	400 r	10	4000 r	46-54
6.	500 r	7-8	3500 r-4000 r	32-44
7.	600 r	6-7	3600 r-4200 r	27-38

\* Out-patients were treated five days per week and in-patients six days per week previous to July 1947. Since that date all patients are treated five days per week.

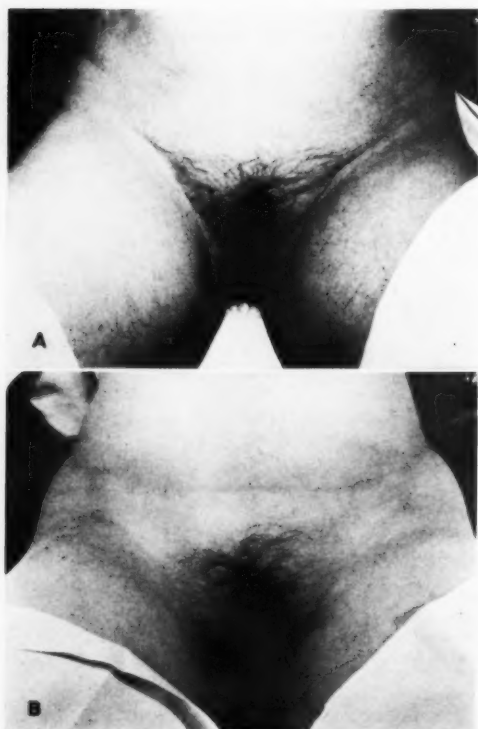


Fig. 3. Influence of size of increment and time spacing on skin and subcutaneous reactions.

A. M. B., three years after treatment: 100 r to four ports each day; 400 kv. (h.v.l. 5.0 mm. Cu); 4,242 r total dose (exit plus incident) to each port within 48 days). Minimal changes.

B. M. W., eighteen months after treatment: 400 r to one of four ports each day; 400 kv. (h.v.l. 5.0 mm. Cu); 4,160 r total dose (exit plus incident) to each port within 49 days. Minimal-plus changes.

for the same total skin roentgens (incident plus exit dose) whether the radiation was given to four ports per day, or one of four ports per day every fourth day. The degree of erythema at the end of treatment, although varying in any one technic group because of individual sensitivity, was less intense for the small increments, line 1, than for the large increments, lines 3 and 4 in Table I.

The late skin and subcutaneous changes were also more severe in the large-increment group than in the small-increment group. This is demonstrated as follows:

100 r to 4 ports per day.....Minimal  
400 r to 1 of 4 ports per day...Minimal plus to moderate

125 r to 4 ports per day.....Minimal to moderate  
500 r to 1 of 4 ports per day...Moderate plus to severe  
150 r to 4 ports per day.....Minimal plus to moderate  
600 r to 1 of 4 ports per day...Severe

The terms used to describe the late skin and subcutaneous changes may be defined in the following way:

*Minimal:* Slight dryness, mild pigmentation, epilation. (Not permanent.)

*Moderate:* Dryness, pigmentation, slight atrophy, occasional mild telangiectasis, mild subcutaneous fibrosis without fixation, epilation.

*Severe:* Dryness, pigmentation, atrophy, scarring, telangiectasis, subcutaneous fibrosis with fixation, epilation. (Permanent.)

An example of each of the above reactions is shown in Figures 3, 4, and 5.

It was also observed that for comparable roentgen doses, especially when increments of 500 r or 600 r were applied to one skin port per day, the 200-kv. radiation gave somewhat more intense late changes (telangiectasis, atrophy, scarring, and subcutaneous fibrosis) than either the 400-kv. or the 1,000-kv. radiation. From this study it is felt that 150 r to four ports each day for thirty cycles of treatment within forty-two days gives a very desirable depth dose-time spacing ratio with a safe immediate normal tissue reaction followed by mild late normal tissue effect. However, to test a larger daily increment to four or six ports each day in a shorter interval, a group of patients is now receiving 175 r to two anterior ports, two posterior ports, and sometimes two lateral ports each day for an average total of 25 cycles within thirty-three to thirty-five days. This permits an average tumor dose of 5,000 to 6,000 r to cervix and parametrial areas. So far, the reaction at the end of treatment is moderate in intensity, and the skin and subcutaneous changes four to eight months later are moderate.

### III. COMPARISON OF REACTIONS PRODUCED BY EQUAL DOSES OF 1,000-KV. AND 200-KV. RADIATION

It has generally been accepted that with increasing hardness of radiation above 3.0

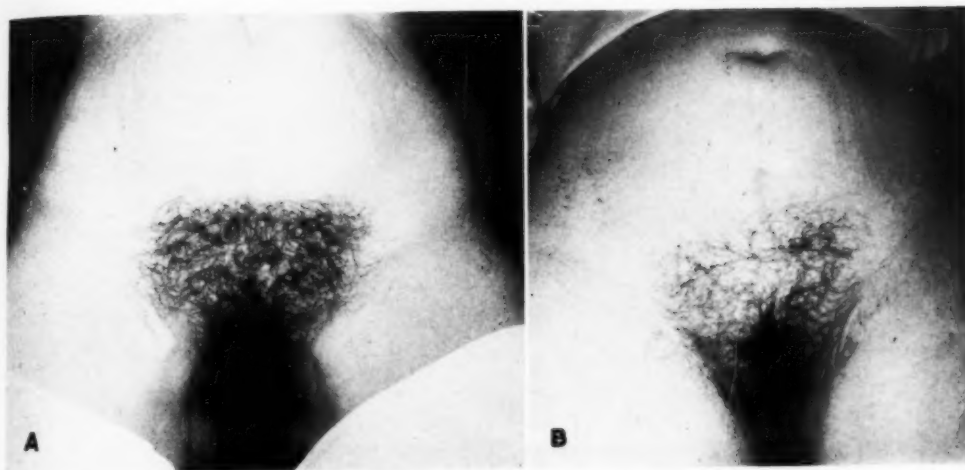


Fig. 4. Influence of size of increment and time spacing on skin and subcutaneous changes.

- A. V. W., eighteen months after treatment: 125 r to four ports each day; 200 kv. (h.v.l. 0.9 mm. Cu); 4,128 r total dose to each port (incident plus exit) within 47 days. Minimal changes.  
 B. E. W., three years after treatment: 500 r to one of four ports each day; 200 kv. (h.v.l. 0.9 mm. Cu); 3,930 r total dose to each port (incident plus exit) within 46 days. Moderate-plus changes.



Fig. 5. Influence of size of increment and time spacing on skin and subcutaneous changes.

- A. E. F., fifteen months after treatment: 150 r to four ports each day; 1,000 kv. (h.v.l. 9.0 mm. Cu); 4,410 r total dose to each port (incident plus exit) within 40 days. Moderate-plus changes.  
 B. M. A., thirty-one months after treatment: 600 r to one port each day; 1,000 kv. (h.v.l. 9.0 mm. Cu); 4,452 r total dose to each port (incident plus exit) within 43 days. Severe changes.

mm. Al h.v.l. there is a corresponding increase in the total number of roentgens the skin will tolerate. In other words, a roentgen at the higher qualities is believed to be less efficient in producing human skin reactions than the lower qualities. The results obtained by Stone and Robinson (1) tend to confirm this statement. On the other hand, it has been our experience that in the daily routine treatment of

patients, where a cross-fire treatment technic is used and the radiation is divided over several weeks, there is no significant difference in the total dose (incident plus exit) delivered and no essential difference in the reactions produced by the three qualities of radiation. The similarity in immediate reactions produced by equal total doses of the three qualities could be due in part to the biological variation and in part

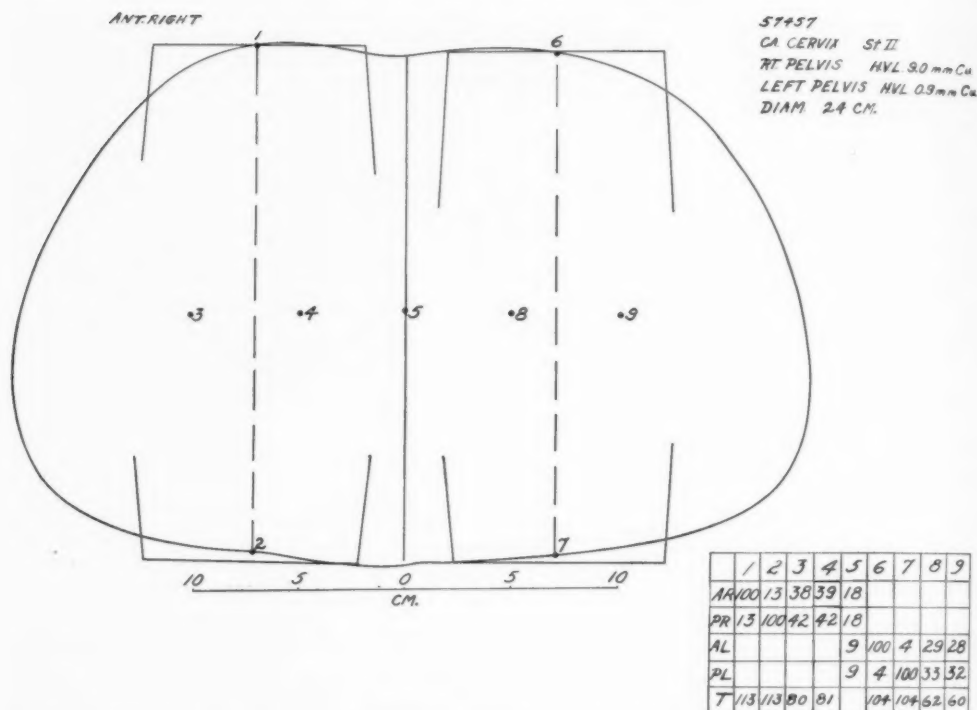


Fig. 6. Treatment technic diagram. Right pelvis, 1,000 kv. (h.v.l. 9.0 mm. Cu). Left pelvis, 200 kv. (h.v.l. 0.9 mm. Cu).

to variations in the daily increment and time spacing. Therefore, in order to eliminate these variables, the following program was set up. Each patient was treated with two different qualities of radiation. The patients selected were of necessity mostly those with advanced cancer (uterine and metastatic breast), yet who were in sufficiently good physical condition to permit return for periodic examination following treatment. The skin was used as the unit of comparison because it is the most constant and accessible part of the human body for such a study. Even though the visual and palpable interpretation of biological reactions may be open to error, these human senses must remain the prime tools in the everyday routine examination of any patient.

After a life-size diagram of the level of treatment had been made, isodose charts were used to determine the exit percentage

in relation to the incident skin dose (see Fig. 6). The right side of the pelvis was used for the 1,000-kv. and the left side for the 200-kv. radiation. The skin fields, both anterior and posterior, were separated by 4 cm. so that back-scatter would not be contributed from one side to the other. The percentage radiation reaching the exit ports was determined. The incident increment was adjusted so that each of the four ports received an equal number of roentgens. In other words, since the 1,000-kv. exit percentage was higher than the 200-kv., the 200-kv. increment was increased so that, when it was added to its exit contribution, the sum would equal the total of the 1,000 kv. (increment plus exit). In this manner, the increments in roentgens delivered each day with two different qualities were different, but after one complete cycle (all four ports having been treated), the total dose to the skin was equal.

TABLE II: SKIN AND SUBCUTANEOUS REACTIONS

Group	Last Day of Treatment	Four or More Months Later
<i>A. 100 r</i>		
F. M.	Equal	Equal (16 mo.); then retreated
E. H.	More with 1,000 kv. (died 2 mo.)	.....
O. S.	Equal	Equal (7 mo.; died)
V. B.	Equal	Equal (48 mo.)
E. W.	More with 1,000 kv.	More with 1,000 kv. (died 4 mo.)
S. R.	Equal	Equal (72 mo.)
<i>B. 200 r</i>		
J. M.	Slightly more with 200 kv.	Equal (9 mo.; died)
B. W.	More with 200 kv.	More with 200 kv. (60 mo.)
<i>C. 300 r</i>		
M. B.	Slightly more with 200 kv.	More with 200 kv. (8 mo.) (died 15 mo.)
L. R.	Equal	Equal (12 mo.); then retreated
N. R.	Equal	Equal (72 mo.)
C. E.	Equal	Equal (5 mo.; died)
A. P.	Equal	Equal (14 mo.; died)
<i>D. 400 r</i>		
M. W.	Very slightly more with 1,000 kv.	Equal (30 mo.)
S. K.	Equal	More with 200 kv. (8 mo.; retreated)
<i>E. 500 r</i>		
H. K.	Equal	More with 200 kv. (30 mo.)
E. N.	Equal	More with 200 kv. (12 mo.)
L. R.	Equal	More with 200 kv. (5 mo.). Last note died 1 year
G. B.	Equal	Slightly more with 200 kv. (3 yr.)
<i>Summary</i>		
Equal	13	10
More with 1,000 kv.	3	1
More with 200 kv.	3	7

Because in routine radiation therapy the total roentgen dose to one port in any specified treatment period must be considered an important item, so in this study the total roentgen dose and the time period of delivery remained identical for either quality in any one treatment. Of course, the quality of the exit beam will be altered in both instances. Nevertheless, the number of exit r was added to the number of incident r, without regard to the differences in quality. While the influence of bone absorption and scattering is more marked with radiation generated by 200 kv. than by 1,000 kv. (Stenstrom and Marvin, 2), no compensation was made for this difference in these dosage studies.

The cases listed in Table II were treated according to groups as follows:

- A. 100 r to four ports each day. .... 6 cases*  
*Example, S. R., carcinoma of cervix, Stage IV.*  
 A-P diameter, 19 cm.  
 8/5/43 Anterior right pelvis ..... 1,000 kv., 100 r  
 Posterior right pelvis ..... 1,000 kv., 100 r  
 Anterior left pelvis. . . 200 kv., 107 r  
 Posterior left pelvis. . . 200 kv., 107 r



Fig. 7. Influence of quality of radiation on skin and subcutaneous reactions. Immediate identical skin reactions on last day of treatment. Total dose per port, 4,920 r. Total time, 51 days. 1,000-kv. increment, 100 r. 200 kv. increment, 107 r. This patient had barely discernible skin changes on both right and left sides six years later.

Total skin dose to each port after one cycle ..... 123 r  
 Field size 10 X 15 cm.  
 9/23/43 (last day of treatment). Forty cycles within 50 days.

Total dose to each skin port. .4,920 r  
 Total dose to center of pelvis .2,000 r



Fig. 8. Influence of quality of radiation on skin and subcutaneous reactions. Unequal reactions five years following treatment. The 200-kv. side shows telangiectasis, atrophy, scarring and subcutaneous fibrosis whereas the 1,000-kv. side shows minimal changes. Total dose per port, 3,712 r. Total time, 47 days. 1,000-kv. increment, 200 r. 200-kv. increment, 214 r.

Total dose 5 cm. to right of center.....4,000 r  
Total dose 5 cm. to left of center.....3,724 r

Skin showed equal reaction on the last day of treatment and two months later. Six years later there is no difference in the condition of the skin or subcutaneous tissue (Fig. 7). Patient alive without disease to date. Radium on 9/24/43, 3,820 gamma r at 2 cm. Radon seeds 12/21/43, 1,064 mc. hr.

**B. 200 r to two ports each day.....2 cases**  
*Example, B. W., carcinoma of cervix, Stage I.*

A-P diameter, 22 cm.

1/18/43 Anterior right pelvis  
1,000 kv., 200 r  
Anterior left pelvis.. 200 kv., 214 r  
1/19/43 Posterior right pelvis.....1,000 kv., 200 r  
Posterior left pelvis. 200 kv., 214 r  
Total skin dose to each port after one cycle.....232 r  
Field size 10 × 15 cm.  
3/5/43 (last day of treatment). Sixteen cycles within 48 days  
Total dose to each port....3,712 r  
Total dose to center of pelvis.1,744 r  
Total dose 5 cm. to right of center.....2,848 r  
Total dose 5 cm. to left of center.....2,397 r

On last day of treatment the anterior reaction is slightly more intense on the 200-kv. side, while posterior reactions are equal. Six months after treatment, very slightly more pigmentation on left side (200 kv.). Five

years later, more changes left anterior (200. kv.)—telangiectasis, atrophy and subcutaneous fibrosis (Fig. 8). Posterior ports equal. Patient alive with no evidence of disease to date. Radium to cervix 3/5/43, 3,700 gamma r at 2 cm.

**C. 300 r to two ports each day.....5 cases**

*Example, M. B., carcinoma of breast metastatic to pelvis. A-P diameter, 18 cm.*

3/16/43 Anterior right pelvis  
1,000 kv., 300 r  
Anterior left pelvis.. 200 kv., 325 r  
3/17/43 Posterior right pelvis.....1,000 kv., 300 r  
Posterior left pelvis. 200 kv., 325 r  
Total skin dose to each port after one cycle.....381 r  
Field size 10 × 15 cm.  
4/12/43 (last day of treatment). Ten cycles within 28 days  
Total dose to each skin port..3,810 r  
Total dose to center pelvis...1,490 r  
Total dose 5 cm. to right of center.....3,420 r  
Total dose 5 cm. to left of center.....3,090 r

Two weeks and eight months following treatment the reaction was practically identical (Fig. 9). Patient died of lung metastases on 6/22/44.

**D. 400 r to two ports each day.....2 cases**

*Example 1, S. K., carcinoma of cervix, Stage II.*

A-P diameter, 24 cm.

7/9/46 Anterior right pelvis  
1,000 kv., 400 r  
Anterior left pelvis.. 200 kv., 435 r  
7/10/46 Posterior right pelvis.....1,000 kv., 400 r  
Posterior left pelvis. 200 kv., 435 r  
Total skin dose to each port after one cycle.....452 r  
Field size 10 × 15 cm.  
7/31/46 (last day of treatment). Ten cycles within 23 days  
Total dose to each skin port..4,520 r  
Total dose to center of pelvis.....2,220 r  
Total dose 5 cm. to right of center.....3,240 r  
Total dose 5 cm. to left of center.....2,480 r

On last day of treatment reactions identical. Eleven months after treatment the 200-kv. (left) side showed much more scarring, atrophy and subcutaneous fibrosis (Fig. 10).

Radon seeds to cervix, 3,280 gamma r at 2 cm. on 7/8/46, radium tubes to cervix, 5,460 gamma r at 2 cm., on 8/30/46. Supplemental x-ray (h.v.l. 5.0 mm. Cu) to pelvis 3/13/47 to 4/7/47 with 2,288 r to center of pelvis. Patient expired 11/25/47.

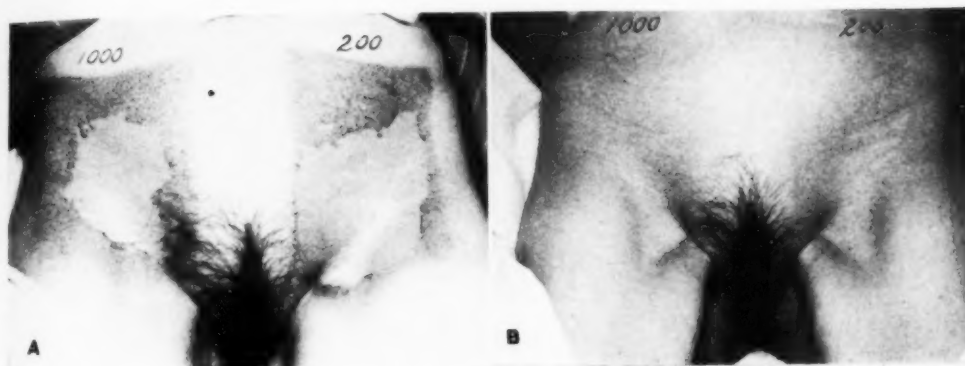


Fig. 9. Influence of quality of radiation on skin and subcutaneous reactions.

A. Immediate reaction slightly more on the 200-kv. side.

B. Reactions almost identical 8 months following treatment.

Total dose per port, 3,810 r. Total time, 28 days. 1,000-kv. increment, 300 r. 200-kv. increment, 325 r.

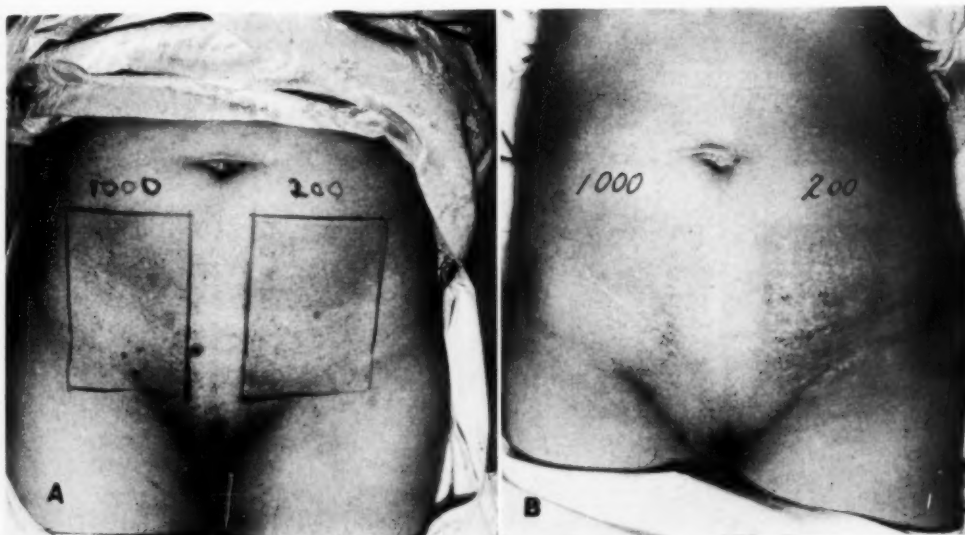


Fig. 10. Influence of quality of radiation on skin and subcutaneous reactions.

A. Immediate reactions identical on last day of treatment.

B. More marked reaction on 200-kv. side 11 months following treatment.

Total dose per port, 4,520 r. Total time, 23 days. 1,000-kv. increment, 400 r. 200-kv. increment, 435 r.

Example 2, M. W., carcinoma of cervix, Stage

III. A-P diameter, 24 cm.

6/13/46 Anterior right pelvis

1,000 kv., 400 r

Anterior left pelvis. 200 kv., 437 r

6/14/46 Posterior right pel-

vis. 1,000 kv., 400 r

Posterior left pelvis. 200 kv., 437 r

Total skin dose to each port after

one cycle. 468 r

Field size 10 X 15 cm.

7/6/46 (last day of treatment). Ten cycles within 24 days

Total dose to each skin port. 4,680 r

Total dose to center of pelvis. 2,160 r

Total dose 5 cm. to right of

center. 3,680 r

Total dose 5 cm. to left of

center. 3,146 r

On last day of treatment there was slightly more reaction on right or 1,000-kv. side (Fig. 11). Two and one-half years after treatment,

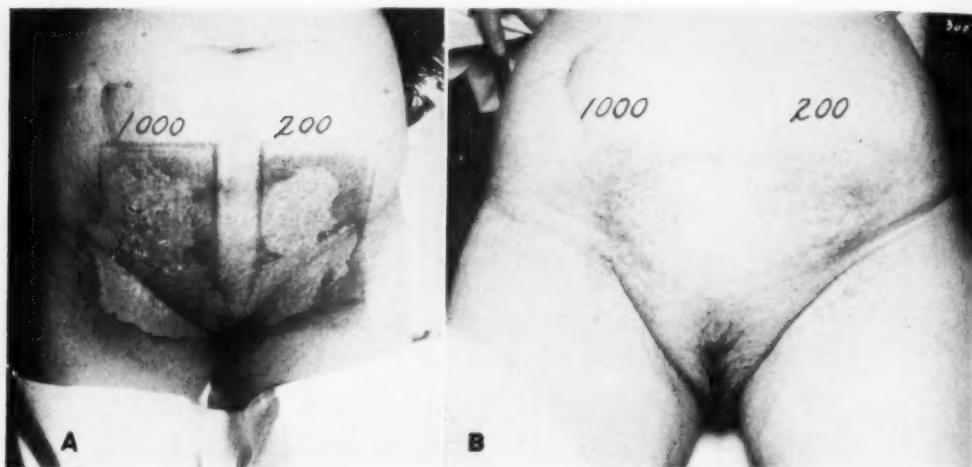


Fig. 11. Influence of quality of radiation on skin and subcutaneous reactions.

A. Reaction slightly greater on the 1,000-kv. side one month following treatment.

B. Skin changes similar two and one half years later. The 1,000-kv. side shows slightly more subcutaneous fibrosis.

Total dose per port, 4,680 r. Total time, 24 days. 1,000-kv. increment, 400 r. 200-kv. increment, 437 r.



Fig. 12. Influence of quality of radiation on skin and subcutaneous reactions.

A. Similar reactions four weeks after treatment.

B. The 200-kv. side shows more scarring, telangiectasis, and subcutaneous fibrosis one year after treatment.

Total dose per port, 4,680 r. Total time, 20 days. 1,000-kv. increment 500 r. 200-kv. increment, 537 r.

the skin reactions were similar, although there was very slightly more subcutaneous fibrosis on the 1,000-kv. anterior side. Posterior ports almost identical.

6/3/46 2,360 gamma r at 2 cm., from radon seeds, and 5,400 gamma r at 2 cm., from radium tubes.

E. 500 r to two ports each day. . . . . 4 cases

Example 1, E. N., carcinoma of cervix, Stage II.

A-P diameter, 22 cm.

8/15/46	Anterior right pelvis	1,000 kv., 500 r
	Anterior left pelvis..	200 kv., 537 r
8/16/46	Posterior right pel-	
	vis.....	1,000 kv., 500 r
	Posterior left pelvis.	200 kv., 537 r
	Total skin dose to each port after	
	one cycle.....	585 r
	Field size 10 × 15 cm	

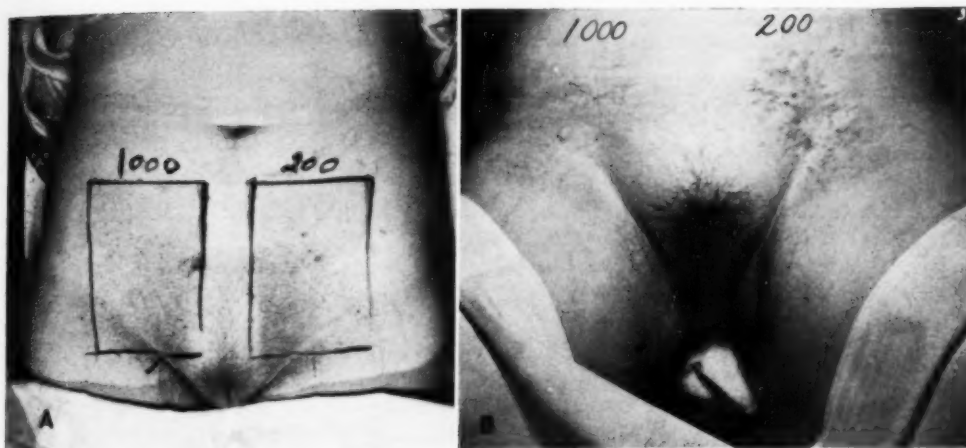


Fig. 13. Influence of quality of radiation on skin and subcutaneous reactions.

A. Immediate similar reactions on last day of treatment.

B. Three years later the 200-kv. side shows more telangiectasis, atrophy, scarring, and subcutaneous fibrosis. Total dose per port, 4,760 r. Total time, 23 days. 1,000-kv. increment, 500 r. 200-kv. increment, 536 r.

9/3/46 (last day of treatment). Eight cycles within 20 days

Total dose to each skin port. 4,680 r

Total dose to center of pelvis. 2,496 r

Total dose 5 cm. to right of

center.....3,440 r

Total dose 5 cm. to left of

center.....3,008 r

On last day of treatment the skin reactions were identical, but mild. Three weeks later the skin reactions were almost identical but severe. One year later there was more scarring, atrophy, and subcutaneous fibrosis on the 200-kv. side (Fig. 12).

8/8/46-8/14/46 6,650 gamma r at 2 cm., from radium. Death 12/8/47 from abdominal metastases.

Example 2, H. K., carcinoma of cervix, Stage II.

A-P diameter, 20 cm.

9/6/46 Anterior right pelvis

1,000 kv., 500 r

Anterior left pelvis.. 200 kv., 536 r

Posterior right pel-

vis.....1,000 kv., 500 r

Posterior left pelvis. 200 kv., 536 r

Total skin dose to each port after

one cycle.....595 r

Field size 10 X 15 cm

9/26/46 (last day of treatment). Eight cycles within 23 days

Total dose to each skin port. 4,760 r

Total dose to center of pelvis. 2,312 r

Total dose 5 cm. to right of

center.....3,960 r

Total dose 5 cm. to left of

center.....3,432 r

On last day of treatment skin reactions identical but mild. Ten months after treatment more atrophy and subcutaneous fibrosis on 200-kv. side. Three years later more scarring, fixation, and telangiectasis on 200-kv side, especially anteriorly (Fig. 13). 8/30/46 to 9/3/46 5,850 gamma r at 2 cm., from radium. Patient alive with no evidence of disease to date.

It is clear from studying the 19 cases shown in Table II that the reactions of the skin at the end of the treatment were similar in 13 of the cases. Of the 3 cases showing more erythema on the 1,000-kv. side, 2 were in the 100-r group and 1 in the 400-r group. Of the 3 cases showing more reaction on the 200-kv. side at the end of treatment, 2 were in the 200-r group and 1 in the 300-r group.

The reaction after four months was similar in 10 cases, slightly more on the 1,000-kv. side in 1 and definitely more on the 200-kv. side in 7. One patient in the 100-r group, who showed more immediate effect on the skin from the 1,000-kv. beam, lived only two months after treatment; hence no observation later than two months was possible. All the cases in the 500-r group showed more late reaction on the 200-kv. side.

TABLE III: COMPARISON OF DEPTH DOSAGES IN DIFFERENT GROUPS

Group	Av. Total Dose to 1 Skin Port	Av. Treatment Time (days)	Av. Mid-Depth Dose 200 kv.	1,000 kv.	Increase over 200 kv., %
A. 100 r	4,631 r	55.0	2,891 r	3,516 r	21.6
B. 200 r	3,736 r	46.5	2,587 r	3,049 r	17.8
C. 300 r	4,151 r	30.8	2,785 r	3,284 r	17.9
D. 400 r	4,600 r	24.0	2,875 r	3,493 r	21.4
E. 500 r	4,720 r	19.7	3,308 r	3,780 r	14.3
Average					18.6

One should note that the time period over which these doses were applied varied inversely with the size of the increment (Table III). In actual routine treatment, such intensive dose technics as given in these experimental 400-r and 500-r groups are not used.

These findings show that one cannot judge the radiation effect only from reaction at the end of the treatment, but must anticipate changes of note many months or years later. Since 5 out of 7 of the cases showing more late reaction on the 200-kv. side were in the 400-r or 500-r group, it is quite apparent that such intensive dosage increments served to cause tissue changes severe enough to distinguish a biological difference in the two radiation qualities as applied to cross-fire technic.

#### IV. DEPTH DOSES AND REACTIONS WITH THREE QUALITIES OF RADIATION

Associated with the higher-voltage therapy is the increase in depth dose. The same source of information which was used for the skin dosage in Part I was used to obtain the depth dosages. A point 2 cm. lateral to the cervical canal and midway in the anteroposterior dimension was selected as the point for the estimation of the x-ray dosage. The total dose in roentgens was plotted against the treatment time in days, as shown in Figure 14. The points scatter more widely than do the skin dosage values and the curves represent the mid-line of the points shown.

It is evident from these curves that there is a decided increase in the depth dosage with the 1,000-kv. radiation over that with 200 kv. The 400-kv. radiation dosage curve is intermediate between the other two. At the forty-fifth day of treatment, at which time there is the greatest cluster of points,

there was 20.4 per cent more 1,000-kv. radiation delivered to the reference point than with 200-kv. radiation, and similarly there was 18.5 per cent more 400-kv. radiation than with 200 kv. The depth dose increase over the skin dose at the forty-fifth day is as follows:

1,000 kv.: 25.6 per cent more in depth than on skin  
400 kv.: 11.6 per cent more in depth than on skin  
200 kv.: 10.5 per cent more in depth than on skin

At a later date the comparative reactions in the depth, as manifested by clinical end-results, will be reported. Not enough time has transpired to compare the depth reactions with different technical attacks (*e.g.*, varying increments, cycles, and qualities). To date the impression is that there are more immediate and late bladder-rectal complications when 1,000-kv. x-rays are used.

Since the total r dose to the point 2 cm. lateral to the cervix has been kept to an average of 8,000 to 9,000 total r (x- plus gamma rays), and since the gamma r dose in the 1,000-kv. group was smaller than in the 200-kv. group because of the greater x-ray dose delivered to the depth, such findings as above must be due to the greater sensitization of the bladder or rectal mucosa to even smaller gamma doses. This could occur through the greater vascular changes due to the much larger x-ray doses delivered throughout the pelvic tumor area as well as the contiguous normal tissue bed. It is reasonable to assume that if the skin and subcutaneous tissue changes are somewhat similar with 200-kv. and 1,000-kv. radiations when routine cross-fire methods are employed, then the delivery of 20 per cent more radiation in the depth by 1,000-kv. x-rays could create such changes as mentioned.

se over  
v., %  
6  
8  
9  
4  
3  
6

00-kv.  
point  
anilarly  
radia-  
h dose  
y-fifth

on skin  
on skin  
on skin

reac-  
clinical  
nough  
depth  
attacks  
d qual-  
s that  
adder-  
x-rays

2 cm.  
to an  
x- plus  
r dose  
han in  
greater  
, such  
greater  
rectal  
doses.  
vascu-  
x-ray  
pelvic  
normal  
assume  
tissue  
00-kv.  
routine  
en the  
in the  
ce such

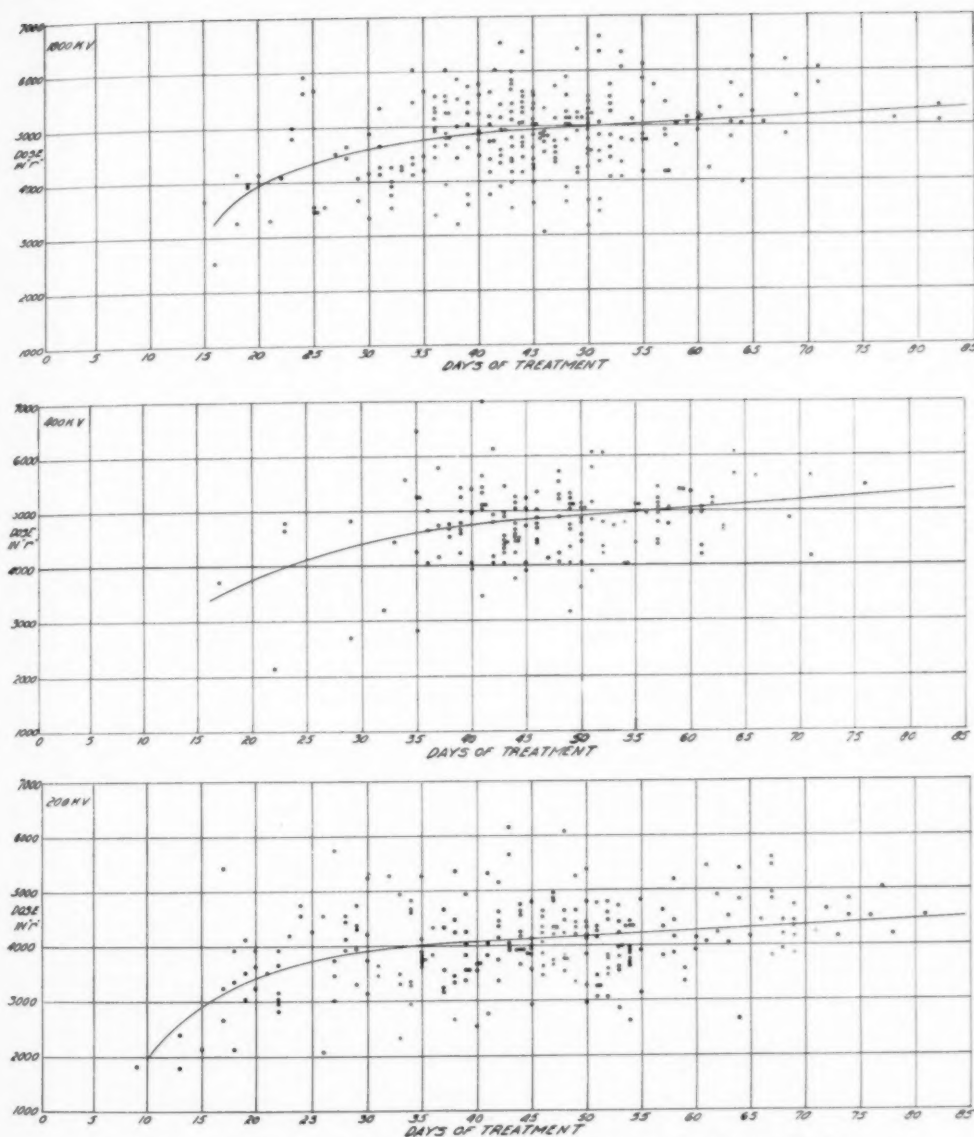


Fig. 14. Depth dose and time relationship in a routine series of pelvic irradiations.

#### V. THE END-RESULTS OF TREATMENT IN CARCINOMA OF THE CERVIX WITH THREE QUALITIES OF RADIATION

Although insufficient time has elapsed to have an adequate number of patients on whom five-year end-results may be reported, it is possible to report three-year end-results in a group which has been

treated with the three qualities of radiation, *i.e.*, 0.9 mm. Cu h.v.l., 5.0 mm. Cu h.v.l., and 9.0 mm. Cu h.v.l., and endeavor to draw some conclusions. The cases selected were cervix carcinomas treated during the years 1939-45, inclusive. This group was chosen because it represents one of the largest single groups of radio-

TABLE IV: OVER-ALL THREE-YEAR END-RESULTS IN CERVIX CARCINOMA, 1939-45

Stage	Treated	Per cent of Total	No Evidence of Disease	Alive with Disease	Died of Disease	Died of Other Causes	Lost	Relative Cure Rate, %
200 kv.								
I	158	17.7	114	7	25	5	7	72.0
II	434	48.7	197	19	178	15	25	45.5
III	181	20.3	56	6	107	2	10	30.9
IV	118	13.3	17	4	89	0	8	14.4
Total	891		384					43.1
400 kv.								
I	9	11.4	8	0	0	0	1	88.9
II	42	53.2	22	2	14	2	2	52.5
III	14	17.7	3	1	10	0	0	17.0
IV	14	17.7	3	0	10	0	1	17.0
Total	79		36					45.5
1,000 kv.								
I	14	8.3	9	0	3	0	2	64.3
II	73	43.5	47	1	23	0	2	64.3
III	41	24.4	15	0	26	0	0	36.6
IV	40	23.8	11	1	26	1	1	27.5
Total	168		82					48.8

logical cases admitted to this hospital. During these years there were 891 cervix cases treated with 200-kv., 79 with 400-kv., and 168 with 1,000 kv.-radiation. Table IV gives the over-all cure rate for the three qualities of radiation.

It is evident from Table IV that when the end-results are compared, there is a very slightly progressive increase in the cure rate with increasing quality of radiation. However, a comparison based on the above material does not necessarily present the true picture, for several reasons. (a) The distribution of patients in the clinical stages of the disease is not the same for the different qualities of radiation. For example, a greater percentage of the more hopeful cases (Stages I and II) and a smaller percentage of those which were more hopeless (Stages III and IV) were treated with 200-kv. therapy than with 1,000-kv. Had the distribution between the two qualities been the same, it is reasonable to conclude that the difference in the end-results would have been more marked in favor of 1,000 kv. (b) The relative number of patients who died of other causes, as well as those who were lost to follow-up, is not the same for the three qualities. (c) There was a definite endeavor to treat those patients who had a

greater anteroposterior dimension with the higher voltages. Had these patients been treated with the lower quality, there would have been a smaller dose delivered to the tumor area.

Because of the smaller number of cases treated with 400-kv. therapy, this group has been eliminated from any further study in this paper.

In order to analyze further the data presented in Table IV, it was decided to be more rigorous in selecting the cases. Therefore, all patients lost to follow-up or having died of other causes prior to the three-year limit were eliminated entirely. For a comparative radiation study of this type, such eliminations are justifiable, because it is impossible to evaluate the status of such patients with regard to the results of irradiation. All Stage I and Stage IV cases were eliminated, because there was the greatest discrepancy in the incidence of these two stages of the disease. The total number of Stage I cases was smaller and in many cases of this stage the radium alone could account for the survival. Stage IV, because of the nature and spread of the disease, does not lend itself to a radiation study. Finally, the cases treated by x-rays alone were eliminated.

After eliminations, only those patients

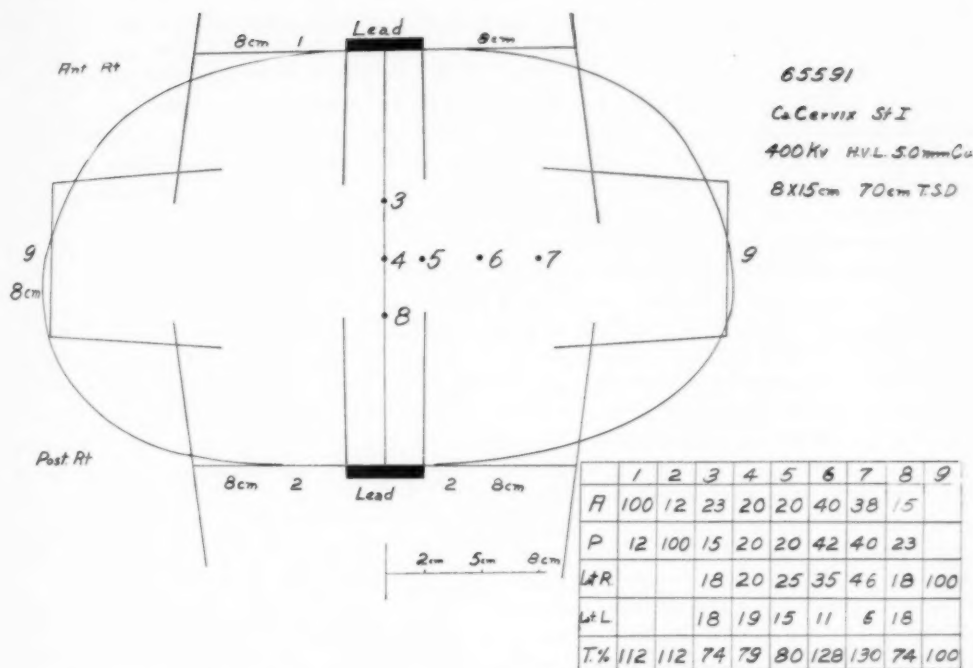


Fig. 15. Treatment technic diagram. X-ray tube target is centered over the mid-line lead strip separating two 8 x 15-cm. skin ports. The center and 2 cm. lateral to the center depth points receive 60 per cent less x-ray than the 5 cm. and 8 cm. lateral points.

were considered who were treated with intracavitary radium and/or interstitial radon in addition to the external application of x-radiation according to the following technic: a four-field set-up with two anterior and two posterior narrow rectangular fields, angulated toward the mid-line; technic determined by life-size contour drawings of pelvis and isodose chart manipulation. All of the patients requiring retreatment at a later date, even though free of disease following supplemental therapy, were considered as representing failures of the primary course of treatment, and are included with those who are alive with disease and died of the disease.

There were 92 cases in this restricted group which were treated with 200-kv. radiation and 89 cases which were treated similarly with 1,000-kv. radiation. The three-year cure rate is 45.6 per cent for the lower quality and 58.5 per cent for the higher-voltage therapy, an improvement of

28 per cent. Although the results are not statistically significant because of the small numbers, nevertheless they are definitely impressive. The improvement with the higher voltages could be attributed to the increase in tumor dose delivered by that quality. To demonstrate this conclusion, a break-down of the cases into progressive x-ray dosage brackets is indicated. However, again because of the small number of cases involved, this type of break-down was reserved until more patients have been treated, so as to yield results which will have significance.

It has also been noted that there have been fewer local recurrences in the cervix area when the x-ray r dose and gamma r dose were of a ratio 1:1 to 1:3 instead of 3:1. This increase of the gamma r over the x-ray r shortens the over-all treatment period, hence increasing the intensity of the radiation regime. With this information in mind, the technical approach to

cervix cancer has been altered recently as follows: In Stage I and Stage II cases (League of Nation classification) diverging right and left anterior and posterior ports and converging lateral ports are used. The anterior and posterior ports are separated by 3 to 5 cm. of lead, depending upon the size of the patient and the quality of the radiation. For the anterior and posterior fields, the target of the tube is centered over the lead (Fig. 15). A dose of approximately 2,000 r is applied to the point 2 cm. lateral to the cervical canal. At the present time an increment of 175 r is given to all ports each day. At the end of the x-ray course of treatments, a gamma r dose of approximately 6,000 r is given to the same point, making a ratio of x-ray r to gamma r of 1:3. The points 5 and 8 cm. lateral to the cervical canal will receive a combined total dose of 4,000 to 5,000 r, depending on the size of the pelvis, the quality of the radiation, and the type of radium applicator. The total treatment time is kept within nineteen to twenty-five days. A later supplemental external course of x-ray may be directed to the parametrial structure, if indicated.

In Stage III cases the same x-ray technic of diverging beams is used. In these cases, however, the ratio of x-ray r to gamma r is maintained at 1:1, for a total dose of 8,000 to 9,000 r at the 2 cm. point. This permits a dose of 5,000 to 6,000 r to be delivered to points 5 and 8 cm. lateral to the cervical canal within a total treatment time of thirty-two to thirty-six days.

Converging anterior, posterior, and lateral ports may be necessary in a large pelvis in order to deliver adequate depth dosages. Newly improved radium applicators, designed to increase the gamma r dose to the 5 cm. lateral point, have made the diverging port technic more advantageous.

#### SUMMARY

I. Curves are presented showing the treatment time-skin dose relationship for 200-, 400- and 1,000-kv. radiation.

II. Patients treated with small daily increments through four ports per day

showed less immediate and late skin and subcutaneous reactions than those treated with a technic in which each of four ports received a larger increment every fourth day (one port treated per day). The total treatment time and dosage were the same in the two groups. The late changes, when large increments were used, were more severe and pronounced with the 200-kv. radiation than with 400- or 1,000-kv. radiation.

III. Comparisons of skin and subcutaneous reactions produced in the same patient by 200 kv. and 1,000 kv. showed that for equal total dosage (incident plus exit) and equal treatment time, the immediate reactions were similar in a large percentage of the patients. The 200-kv. radiation, however, produced a greater number of late skin and subcutaneous reactions than did the 1,000-kv. radiation.

IV. Tissue doses at depth as a function of the treatment time for the three qualities of radiation, namely, 0.9, 5.0, and 9.0 mm. Cu h.v.l., are presented graphically. Associated with the increased depth doses of the higher qualities is an increase in the number of bladder and rectal complications.

V. Clinical end-results following irradiation of cervical carcinoma showed the advantage of 1,000-kv. over 200-kv. radiation. This is particularly true in the case of a large pelvis. A selected group of Stage II and Stage III cases showed a three-year controlled disease percentage of 58.5 for 1,000-kv. and 45.6 for 200-kv. radiation. Although these results are not statistically significant, due to the small sample, yet it is felt that they are definitely impressive.

Roswell Park Memorial Institute  
663 North Oak St.  
Buffalo 3, N. Y.

#### REFERENCES

1. STONE, R. S., AND ROBINSON, J. M.: A Comparison of Skin Reactions Produced by 200 Kv. and 1,000 Kv. Radiations. *Am. J. Roentgenol.* **44**: 601-609, October 1940.
2. STENSTROM, K. W., AND MARVIN, J. F.: Ionization Measurements with Bone Chambers and Their Application to Radiation Therapy. *Am. J. Roentgenol.* **56**: 759-770, December 1946.

## SUMARIO

## Algunas Observaciones con Roentgenoterapia de 1,000 kv., 400 kv. y 200 kv.

Las curvas presentadas muestran la relación del tiempo de tratamiento y la dosis cutánea para la irradiación con 200 kv., 400 kv. y 1,000 kv., con capas hemirreductoras de 0.9 mm., 5.0 mm. y 9.0 mm., respectivamente, de cobre, según se usaron en el tratamiento corriente de las neoplasias malignas. Por esas curvas resulta manifestado que, para cualquier período de tratamiento, no hubo diferencia esencial o significativa en la dosis cutánea entregada por las tres clases de radiación.

Las enfermas con carcinoma del cuello uterino tratadas con pequeñas dosis diarias a través de cuatro puertas diariamente revelaron menos inmediatas y tardías reacciones cutáneas y subcutáneas que las tratadas con una técnica en la que cada una de cuatro puertas recibió una dosis mayor cada cuarto día (una puerta tratada al día). En total, el tiempo de tratamiento y la dosis fueron idénticos en ambos grupos. Las alteraciones tardías, cuando se usaron grandes dosis, fueron más intensas con la irradiación de 200 kv. que con la de 400 o de 1,000 kv.

La comparación de las reacciones cutáneas y subcutáneas producidas en la

misma enferma por 200 kv. y 1,000 kv. demostró que con dosis total igual (incidencia más salda) y tiempo de tratamiento igual, las reacciones inmediatas fueron semejantes en un elevado porcentaje de enfermas. La radiación de 200 kv. produjo un número mayor de reacciones tardías que la de 1,000 kv.

Preséntanse gráficamente las dosis histológicas a profundidad como función del tiempo de tratamiento para las tres clases de irradiación. Junto con la mayor dosis a profundidad de las clases más altas va un aumento en el número de complicaciones vesicales y rectales.

Los resultados clínicos terminales consecutivos al tratamiento del carcinoma cervical demostraron la superioridad de la radiación de 1,000 kv. sobre la de 200 kv., en particular en las pacientes de pelvis grande. Un grupo seleccionado de casos de los Períodos II y III reveló un coeficiente de control a los tres años de 58.5 por ciento con la radiación de 1,000 kv. y de 45.6 por ciento con la de 200 kv. Si bien, debido al pequeño número de casos, esos resultados no son estadísticamente significativos, también parece que poseen importancia bien definida.



# Radiation Dosimetry in the Treatment of Functional Thyroid Carcinoma with $I^{131}$

L. D. MARINELLI, M.A.,<sup>2</sup> and RUTH F. HILL

Sloan-Kettering Institute, New York City

AMONG THE SEVERAL factors involved in the therapy of metastatic thyroid cancer with massive doses of  $I^{131}$ , the dose of radiation delivered to lesions and to normal tissues is of particular importance (1). At present, the tissue doses arising from the presence of radio-elements in the body cannot be measured directly *in situ* by ionization methods, but reasonable estimates can be obtained by indirect means. Although these estimates are less precise than those available to conventional radiation therapy, they provide, nevertheless, information which should be useful to the establishment of a rational administration of the isotope and to the correct interpretation of the patient's clinical response.

## THE TUMOR DOSE

It has been shown (2) that the beta radiation dose and the  $I^{131}$  concentration in tissue are related by the following formulae:

$$\text{Total dose} = 18CT_e \text{ er} \dots \dots (1)^3$$

$$\text{Daily dose} = 12.5C \text{ er} \dots \dots (2)$$

In these expressions,  $T_e$  is the effective half-life in days of  $I^{131}$  in the tissue under consideration, *i.e.*, the half-life resulting from both radioactive decay and physiological elimination, and  $C$  is the initial concentration of  $I^{131}$  in microcuries per gram (or millicuries per kilogram) of tissue.<sup>4</sup> Both expressions assume uniform distribution of the isotope in tissue, and,

implicitly, a time of localization which is short compared to  $T_e$ .

In practice, the value of  $T_e$  can be obtained by making repeated measurements of tumor activity with a Geiger-Müller tube placed in a reproducible position, externally to the patient. If the results of these measurements, plotted on a semilogarithmic scale, give a straight line, the effective half-life,  $T_e$ , can be found by simple inspection. If the curve is not a straight line, calculation of the total dose should be done by means of formula (2) and graphical integration.

The value of  $C$  can be obtained by biopsy at a definite time and extrapolated to time of administration by means of the curve described above. This, usually, is the most accurate procedure, but in many cases  $C$  must be determined indirectly; namely, by dividing the  $I^{131}$  content of the tumor by its volume.

The  $I^{131}$  content of the tumor may be obtained sometimes by *in vivo* measurements, as done frequently for the thyroid, or, more often, by subtracting from the dose administered to the patient the amount excreted plus the amount localized in the thyroid (*vide infra*). The tumor volume can be estimated by radiographic methods. The uncertainty which results varies with the case and depends on many factors,<sup>5</sup> but once reasonable values of  $T_e$  and  $C$  are adopted, computation of the radiation dose is straightforward.

<sup>1</sup> This work was supported in part by the Office of Naval Research under contract N6-ORI-99. Accepted for publication in January 1950.

<sup>2</sup> Present address: Argonne National Laboratory, Chicago, Ill.

<sup>3</sup> er (equivalent roentgen) denotes that amount of beta radiation which, under equilibrium conditions, releases in one gram of air as much energy as one roentgen of gamma rays.

<sup>4</sup> In view of doubts concerning the correct disintegration scheme of  $I^{131}$  (3, 4), a millicurie of  $I^{131}$  will be defined for the purpose of this paper as that amount which, as an unfiltered point source, yields a dose rate of 2.7 r per hour of gamma radiation at 1 cm. distance.

<sup>5</sup> In a series of four patients with metastatic lesions, on whom both methods were applied, the tumor concentration, as estimated by indirect means, was found to be 0.32, 4.0, 1.4, and 0.9 times the  $I^{131}$  concentration of biopsied tumor material. It is obvious, therefore, that much room for improvement exists in our present methods of estimating  $C$ .

The tumor dosimetry involved in the treatment of one patient (1) is illustrated in Figures 1A and 1B. The first two doses of  $I^{131}$ , 60 and 125 mc., respectively, were administered orally within one week. Daily measurements of urinary excretion and external measurements over some of the metastases were taken. The upper curve, marked "total  $I^{131}$  in body" (Fig. 1A) represents the total number of millicuries of  $I^{131}$  remaining in the body at any

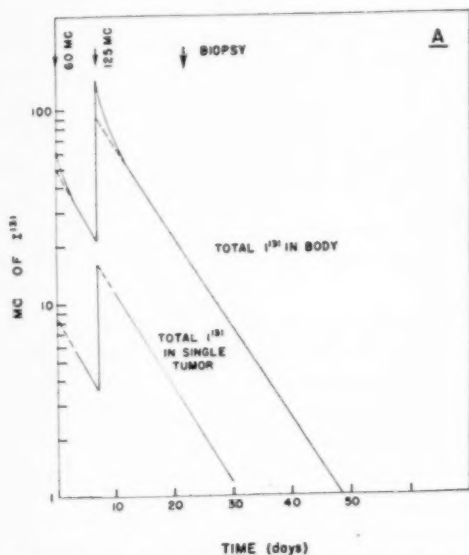


Fig. 1A. Radioactivity in patient F. K. following administration of two doses of  $I^{131}$  seven days apart. The upper curve was obtained by subtracting from the dose administered both radioactive decay and renal excretion. The lower curve was obtained by *in vivo* radioactive measurements over one lesion with a suitably calibrated and shielded Geiger-Müller counter.

time, as a result of both radioactive decay and renal excretion. Except for the first few days following administration, this curve is exponential, the effective half-life being 5.7 days. The curve marked "total  $I^{131}$  in single tumor" (Fig. 1A) is also exponential and parallel to the one for the whole body. This curve was obtained by external measurements over one of the metastatic lesions suitable for this type of study, and it is typical of all the tumors surveyed on this patient following those two doses of  $I^{131}$ . In view of other findings,

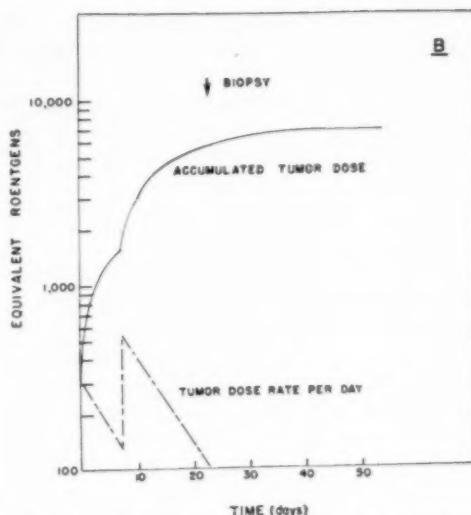


Fig. 1B. Tumor dose rate (er per day), based on total tumor mass of 2.03 kg., and accumulated tumor dose, as a function of time after  $I^{131}$  administration.

such as the low  $I^{131}$  excretion, low thyroid content, and low blood level (less than 1 per cent per kg. after twelve hours), the assumption was made that, except for the first few days, practically all iodine remaining in the body was collected by the tumor tissue. By extrapolating the linear portion of the "body" curve to the time of administration, the iodine collected by all tumor tissue was estimated to be 50 and 90 mc., respectively.<sup>6</sup>

The total tumor mass was calculated to be 2.03 kg. on the basis of biopsy measurements made on the twenty-third day.<sup>7</sup> Applying formula (1), we obtain:

Total dose ( $D_d$ ) =

$$18 \times \frac{50 + 90}{2.03} \times 5.7 = 7,100 \text{ er}$$

<sup>6</sup> This method of estimating total tumor content of  $I^{131}$  is particularly useful in very advanced metastatic cases where the total number of lesions is difficult to establish and the presence of soft-tissue metastases precludes reasonable estimates of tumor dimensions. This procedure finds some support in a recent paper by Keating et al (5), which shows that the  $I^{131}$  fraction unaccounted for by thyroid uptake and renal excretion is about 13 per cent of the administered dose and that this excess decreases at the rate of a few per cent per hour.

<sup>7</sup> The latter calculation consists in dividing the calculated extra-thyroidal  $I^{131}$  remaining in the body at the time of biopsy by the  $I^{131}$  content per gram found in the biopsy specimen.

The tumor dose rate, shown in Figure 1B, in er per day, was calculated by means of equation (2). Thus on the fifteenth day the total tumor content was 38.5 mc.; hence, on the assumption of constant tumor volume,  $C = 38.5/2.03 = 19.0$  mc./kg. and, therefore

$$\text{Daily dose} = 12.5 \times 19 = 237 \text{ er per day}$$

Once the daily dose is obtained, the radiation dose accumulated within any period of time can be computed by simple addition. Figure 1B shows that, in this particular patient, half of the tumor dose was delivered in eleven days, and that the treatment was practically completed in one month.

Before closing this subject, it is fitting to call attention to the additional uncertainty arising in the value of the tumor dose because of the tacit assumption that any one of the methods outlined before yields a value for the  $I^{131}$  concentration which is representative of all metastatic involvement. Previous studies (6-8) have shown that most thyroid tumors are histologically inhomogeneous and that the pattern of  $I^{131}$  deposition is far from uniform. In practice, this factor renders dosimetric estimates of doubtful value except possibly in the unusual instances of homogeneous tumors. However, they remain worthy of consideration, since they do represent a first approximation to the radiation dose. Moreover, they may prove of greater value if some of the procedures which increase  $I^{131}$  pick-up by metastases of thyroid cancer (8, 9) produce also a more uniform distribution of the radio-element.

#### DOSE TO NORMAL TISSUE

From the point of view of the general radiation effect on the patient, it is necessary to consider two further aspects of dosage: (a) that to any other organ or tissue, due to specific concentration; (b) that to the body as a whole, due to the radioactive material circulating in the body fluids.

Since at present no practical means are available to establish routinely the specific concentration of  $I^{131}$  in most tissues of the

individual patient, estimates of normal tissue dose must be based on average results obtained at operation or autopsy or from animal experiments. Unfortunately, no data are available for the marrow, although radiological experience suggests that special attention should be paid to it in matters of general body irradiation. As to the remaining tissues of the body, the available reports (10-13) indicate that  $I^{131}$  concentration in most tissues follows closely the concentration of the blood. The upper alimentary tract and the urinary system, however, should be considered separately because of the high  $I^{131}$  concentration found in stomach juices, saliva (14), and urine.

*For the purpose of this paper, it will be assumed that the dose delivered to the whole body, the mouth, the stomach, and the urinary tract will be equal to that computed on the basis of  $I^{131}$  concentration and turnover in the corresponding bathing liquid available for assay.*

Without entering into detailed consideration of the physical and anatomical factors involved, it should be stated that the calculations based on blood will be fairly representative of whole-body irradiation. Those based on gastric juice, saliva, and urine, on the other hand, will indicate maximal values of the radiation received by very limited regions of the alimentary and urinary tracts.

The results to be presented, therefore, carry a considerable degree of uncertainty in so far as true tissue dose (in er) is concerned. However, they should prove useful in revealing the differences in radiation dose delivered to a particular organ either because of dissimilarity in technic or of individual variations in iodine metabolism. In any case, the extreme conservatism guiding these calculations will serve the therapist with ample warning as to when and where to expect signs of irreversible radiation damage.

Calculations were carried out in the following manner. The concentrations of  $I^{131}$  in the fluids mentioned above were measured for as long a time as possible; they were expressed as microcuries per

gram at the time of sampling (corrected to 100 millicuries administered) and plotted as a function of time (days). Since the dose delivered during the interval in question is proportional to the area under the curve, it is necessary—in order to obtain an answer in er—to compare it to an area which represents a known dose in er. This is readily done by drawing, to the same scale, a rectangle having as sides  $1 \mu\text{c./gram}$  and 1 day, respectively. It is obvious

namely, that the effective half-life was equal to the radioactive half-life of eight days. Hence, the concentration of the last fluid sample was multiplied by  $18 \times 8 = 144$  (equation (1)) and the product added to the value obtained above. This method is illustrated in Figure 2, for the case of patient F. K. It is based on concentrations obtained on whole blood (left-hand scale). To find the dose during each day (or longer period), vertical lines are drawn

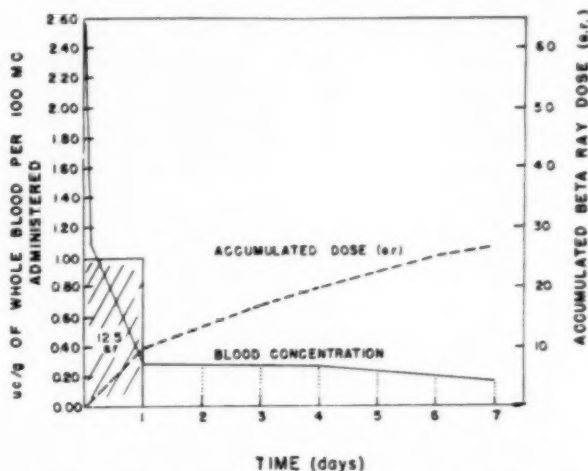


Fig. 2. "Body" dose of patient F. K. referred to 100 mc. of  $I^{131}$ . The abscissa refers to time after isotope administration. The accumulated dose at the end of seven days is 27.7 er. From that time on, to the complete disintegration of the isotope, another 24.5 er will be delivered on the assumption of constant blood concentration. In order to account also for the radiation dose due to the gamma ray of the isotope, the sum  $24.5 + 27.7$  er is multiplied by 1.86, giving a maximum body dose of 97 er (see text).

then, that since the area of this rectangle is  $12.5 \times 1 = 12.5$  er, the area under the concentration curve represents a dose<sup>8</sup>:

$$D_{\beta} = \frac{\text{area under concentration curve}}{\text{area of rectangle}} \times 12.5 \text{ er}$$

In order to account for the radiation delivered after the termination of the test period, the conservative assumption was made that the concentration remained physiologically stable from there on;

<sup>8</sup> 12.5 er is the dose rate per day due to a stable concentration of  $1 \mu\text{c./gram}$ . It would be given in exactly one day if the concentration remained absolutely constant throughout the day.

The dose for the first day (2) due to a physiologically stable concentration of  $1 \mu\text{c./gram}$  at the beginning of the day is  $d\beta = D\beta_d = 144 (1 - e^{-0.003/8}) = 11.95$  er.

from the appropriate points on the "days" axis. The area thus delimited for any period is determined (by counting squares on the original graph) in relation to the area of the reference rectangle (12.5 er). By adding successive daily doses, the cumulative dose curve is obtained for the period of observation (right-hand scale). This is represented by the broken line and reaches 27.7 er (per 100 millicuries) at the end of seven days, when the last blood specimen was obtained. The extrapolation to infinite time is not shown, but amounts to  $0.17 \times 144 = 24.5$  er. The total beta ray dose is, therefore,  $24.5 + 27.7 = 52.2$  er.

TABLE I: ESTIMATED BODY "DOSE" PER 100 MILLICURIES OF  $I^{131}$  ADMINISTERED  
(Based on Blood Concentrations)

Patient, Sex, and Age	Date	Actual Millicuries Administered	Route	Cumulative* Millicuries Administered	Test Period in Days	Equivalent Roentgens (beta plus gamma)		
						24 hr.	at end of 48 hr.	$\infty$
H. H. (M-74)	9/14/46	40	Oral	40	12	18	24	95
	2/20/47	60	Oral	116	7	29	42	99
	2/11/48	200	Oral	365	13	13	24	90
	5/21/48	200	Oral	570	6	9	20	80
F. K. (M-53)	10/2/46	60	Oral	65	7	20	27	97
	5/6/48	314	Oral	805	19	15	22	46
M. A. (F-38)	12/10/47	3†	I. V.	176	2	99	167	
	12/18/47	160	Oral	336	21	38	51	114
	5/14/48	200	Oral	541	25	16	44	318
D. S. (F-40)	2/20/47	60	Oral	63	21	46	64	92
	1/20/48	5	I. V.	586	8	37	44	97
	6/23/48	314	Oral	906	26	25	35	180
P. G. (F-36)	12/18/47	2†	I. V.	193	2	102	189	
	12/31/47	180‡	I. V.	373	9	71	119	196
	5/29/48	250	Oral	638	9	67	118	218
J. A. (M-41)	1/14/48	3	Oral	5	9	22	26	110
L. H. (M-60)	7/31/47	60	Oral	60	5	26	31	70
F. E. (F-69)	2/6/47	0.5	I. V.	3	4	51	71	92
C. C. (M-70)	1/27/48	1	I. V.	1	4	46	59	84
A. F. (M-47)	8/14/48	302	Oral	312	9	28	33	39
V. G. (F-51)	8/2/48	69	Oral	71	9	40	52	88
M. P. (M-58)	6/30/48	225	Oral	304	12	35	45	81
D. K. (F-16)	9/10/48	252	Oral	332	10	12	17	81
L. L.§ (F-54)	10/30/47	99	Oral	381	6	19	33	103
	12/18/47	51	Oral	432	5	59	70	125
A. B. (F-60)	1/13/47	70	Oral	74	18	41	50	65
	2/19/47	99	Oral	242	35	28	44	140
	5/19/48	131	Oral	456	23	50	74	143
L. O. (F-41)	11/20/46	109	Oral	111	15	23	28	122
	12/6/46	65	Oral	176	13	40	68	76
D. K. S. (F-19)	12/29/47	85	Oral	86	18	25	30	59
A. V. (M-46)	7/10/47	48	Oral	51	12	20	24	58
R. A. (F-30)	4/10/47	103	Oral	105	21	28	31	82
D. Y. (F-68)	12/11/46	120	Oral	207	12	27	34	119

\* This includes the dose shown in column 5.

† Test period considered too short to justify extrapolation to infinite time.

‡ Blood concentration obtained by digital puncture.

§ Data on the last 7 patients were made available through the courtesy of Dr. S. M. Seidlin.

The contribution of the gamma rays emitted by  $I^{131}$  to the radiation dose received by the different tissues was based also on the extreme assumption that each organ receives the maximum gamma ray dose which can possibly be delivered at any point in the body, on the assumption that

the  $I^{131}$  concentrated in the body is uniform throughout and equal to that of the blood. For purposes of simplification, the body is represented by a cylinder 60 cm. high and 40 cm. in diameter, and the point of highest gamma ray dose is at its geometrical center (2). At this point, the

contribution of the gamma radiation is 86 per cent of the beta ray dose in the blood but only 10 per cent or less of the maximum beta ray dose delivered to the kidney, stomach, and mouth. In these organs, the gamma ray dose due to the wetting fluid is negligible.

Results of all calculations pertaining to maximum doses in the blood are shown in Table I. Since the concentration of  $I^{131}$  in the blood decreases markedly soon after administration, the doses accumulated in the first twenty-four and forty-eight hours represent, as a rule, the highest dose rates attainable during treatment. Because of their eventual radiotherapeutic interest, they are shown in the table along with other pertinent data.

#### DISCUSSION

*The Blood Dose:* The data shown in Table I were gathered from 34 blood analyses performed on 20 patients. In this group are included 11 analyses on 7 patients made available to the authors through the courtesy of Dr. S. M. Seidlin, Chief of the Medical Physics Research Laboratory, Montefiore Hospital, New York City. In two of the analyses, blood contents of  $I^{131}$  were followed for only two days; hence the blood dose was not estimated beyond the actual period of observation. Of the remaining 32 analyses, 12 were made on 8 male patients, the remaining 20 being obtained from 12 female patients.

*In all instances the table gives the number of roentgens which would have been delivered by a dose of 100 mc. rather than the actual dose delivered.* This is essential if comparisons are to be made, or averages taken. This value may be called the "specific radiation dose" (S.R.D.). It will be noted that this dose varies widely. The ratio between the extremes, calculated for the whole group, is 8.1. If the dose rates of the first two days of treatment are considered, this ratio is somewhat higher, being 11.3 for the dose accumulated within the first twenty-four hours and 11.1 for that obtaining at the end of the first forty-eight

hours. However, if the comparison between extremes is restricted to repeated doses administered to the same patient (M. A., for example), the above mentioned ratios drop considerably; namely, to 2.8 for the total dose, 6.0 for that in the first twenty-four hours, and 3.8 for the dose at the end of forty-eight hours.

In two instances (patients M. A. and P. G.), tracer doses were administered intravenously two weeks before therapy, in an effort to predict accurately the blood dose to be expected from subsequent  $I^{131}$  therapy, and to establish whether intravenous injection would decrease considerably the gastric dose. Unfortunately, blood analyses were not carried beyond the second day. Comparison of the S.R.D. accumulated at this time shows the tracer dose to yield the *higher* value by a factor of 3.3 for the first patient, and 1.6 for the second. These two ratios are not strictly comparable, because the massive  $I^{131}$  administration was oral in one case and intravenous in the other; they indicate, however, that tracer doses should not be expected to predict too closely the  $I^{131}$  content of the blood after intense therapy. In this case, destruction of functional thyroid tissues by radiation has been shown to release, sometimes, an amount of protein-bound iodine which is large when compared to the amount ordinarily circulating in the blood (1, 15). It must be confessed, therefore, that the higher S.R.D.'s obtained with the preliminary tracer doses came as a distinct surprise.

Three other intravenous test doses, given to patients F. E., C. C., and D. S., have resulted, however, in S.R.D.'s considerably lower than the preceding ones, and more in keeping with the average of the whole group. Patients F. E. and C. C. had not previously been given  $I^{131}$  medication comparable to that administered to the first pair of patients, whereas, the other had received more (*vide infra*). A search in the clinical history revealed that renal deficiency would explain the consistently high values obtained in patient P. G., since this patient was found at autopsy to have

extensive metastatic involvement of the kidney, but no similar evidence was found in the case of patient M. A.

Taken as a whole, the group received an average specific radiation dose of 108 er per 100 mc. administered. The entire male group shows an average of 79 er, whereas the female group averages 125.5 er. If, however, the comparison is confined to patients not treated previously with therapeutic doses of  $I^{131}$ , this difference vanishes, the averages being 86 in 7 female patients, and 79 in 7 male patients. The ratio between extreme S.R.D.'s is sharply reduced, being 2.14 for the first, and 2.8 for the second of these selected groups. The data show also that in 5 of 6 female patients (M. A., D. S., P. G., L. L., A. B., and L. O.) on whom repeated blood studies were made, only one (L. O.), failed to show an increase in S.R.D. with the increase of total  $I^{131}$  previously administered. This trend, however, is absent in the 2 male patients (H. H. and F. K.) on whom similar studies were undertaken.

Since the S.R.D. is directly proportional to the fraction of the isotope disintegrating per unit mass of blood, it should be influenced by the following factors: (a) the collection and retention of  $I^{131}$  by functional tissue and its subsequent dilution with the non-radioactive colloid present therein; (b) the excreting efficiency of the kidney and, to a minor degree, that of the skin and gastric mucosa, as affected by circulating  $I^{127}$ , radiation and pathology; (c) the rate of circulatory release of thyroid hormone by functional cancer tissue under irradiation, and its eventual release as iodide by the body tissues under the radiation doses prevailing at these sites during treatment; (d) the  $I^{127}$  intake of the patient throughout the treatment.

Although recent reports (5, 16, 17) throw considerable light on the kinetics of  $I^{131}$  in the body soon after the administration of tracer doses to man, the relative importance of the aforesaid factors under severe therapeutic conditions and for long periods of time remains to be established.

The data presented here merely illus-

trate the degree of uncertainty to be expected from patient to patient and the limited, but definite, usefulness of tracer doses in the evaluation of the S.R.D. for the blood. It is felt, however, that this point merits more exhaustive investigation. It is also evident from these data that temporary cessation of menstruation in some female patients given 200 or more millicuries of  $I^{131}$  may be expected from general body radiation without postulating any particularly high concentrations of  $I^{131}$  in the ovaries.

*The "Kidney" Dose:* As mentioned before, calculations of the kidney dose are based on the concentration of  $I^{131}$  in urine and apply strictly to tissue of the urinary tract which is bathed on all sides by a liquid mass of thickness equal to or greater than the maximum range of the beta particles from  $I^{131}$ , namely, 2 mm. It is obvious that these conditions do not apply to the kidney as a whole and that they may be approached only at the pyramid of this organ or in some foldings of the bladder. It seems more likely that the average kidney dose would be closer to that of the blood, whereas that of the bladder would probably approach less than one-half of the doses estimated on urine concentration.

These doses were calculated in 22 instances in 12 of the patients listed in Table I. The average maximum kidney dose per 100 mc. for the whole group is 757 er; the minimum recorded 351, the maximum reaching 1,366. There is some indication that administration by intravenous route increases this dose, the average being 978 er for a group of 5 assays in 4 patients, but the difference cannot be considered significant. It is characteristic of kidney dosage that a sizable fraction of the total radiation dose (32 to 92 per cent) is delivered in the first forty-eight hours. The ratio of the average "kidney" S.R.D. to that of the blood in the same patients is 6.3, but it may be as high as 13.5 and as low as 2.3 in a single patient. However, when the radioresistance as well as the small fraction of kidney tissue thus irradiated is taken into account, it seems unlikely that

kidney damage will prove to be the immediate limiting factor in the administration of  $I^{131}$  to patients.

*The Dose to Stomach and Mouth:* The geometrical and anatomical factors discussed in connection with the estimate of the dose to the urinary tract apply, in general, to the upper alimentary tract. It is plausible to assume, on these bases, that the doses calculated from gastric juice or saliva measurements are indicative of the maximum dose in some foldings in the mouth and in the pyloric region of the stomach, but that these organs, as a whole, will receive radiation doses not much higher than those given to the body as a whole. The radioactivity of gastric juice was determined in 7 patients; the average maximum "gastric" dose per 100 mc. is 771 er; the minimum recorded 409, the maximum reaching 1,420. Similar computations based on 10 samples of saliva from 8 patients showed an average maximum mouth dose of 2,020 er per 100 mc. administered, the minimum being 787, the maximum going as high as 5,520.

Comparison of total "stomach" dose to total blood dose in the same group of patients yields a ratio of 5.7 on the average, but for a single patient the figure may be as low as 1.3 and as high as 17.0. Similar comparison for the ratio of "mouth" dose to blood dose shows an average ratio of 15.8, the minimum being 4.6 and maximum 69.0.

During the course of these investigations, the question was raised as to the difference in radiation dose to the stomach with intravenous and oral administration of  $I^{131}$ . Since the isotope was administered on a fasting stomach, and since it is also well known that most  $I^{131}$  is absorbed from the gastro-intestinal tract in about an hour (14), it is easy to show that 100 mc. administered in 250 c.c. of water delivered an average dose of roughly 90 er to the stomach. Although this is not an unduly large fraction of the total, it must be realized that it is delivered in a relatively short time.

In two patients, given  $I^{131}$  by intravenous

injection, the gastric S.R.D. obtained was much higher (1,234 and 1,423 er) than in the remainder of the group and more than compensated for the absence of the initial radiation dose due to ingestion. Yet, because of the small number of cases, it cannot be stated categorically that, all things considered, oral administration is the route of choice in the use of massive doses of  $I^{131}$ . In patients on whom separate saliva and gastric juice analyses were done, it was found that  $I^{131}$  concentration in the former was sometimes considerably larger than the latter, but the reverse was never observed. The variations encountered among the stomach doses are similar to those found in blood and kidney; those resulting from saliva assays are more widely scattered.

#### SUMMARY

Description is given of methods by which dosage in  $I^{131}$  therapy can be estimated not only for the tumor but for certain other organs and for the body as a whole. These methods require adaptation to particular cases, but certain common features have been considered. The method of calculation of tumor dose was shown for one individual. A rough estimate of the maximum possible radiation doses delivered to blood, kidney, mouth, and stomach in patients undergoing therapy with  $I^{131}$  has been attempted on the basis of the radioactivity found in blood, urine, saliva, and gastric juice. It is found that, on the average, a total body radiation dose of 108 er results from the administration of 100 mc. of  $I^{131}$ , but that individual variations may shift this value by a factor as great as three in either direction.

For the same amount of  $I^{131}$ , the average maximum "kidney" dose is 757 er; the average maximum "gastric" dose is 771 er, and the average maximum "mouth" dose is 2,020 er. The last three doses, however, must be considered as applying to very limited regions of the organs listed above.

NOTE: The authors take pleasure in acknowledging the technical assistance of the Misses Jane Heslin

and Adelaide Emory, and the co-operation of the Department of Clinical Investigation of the Memorial Hospital Center in securing specimens from the patients under its care. Special thanks are due to Dr. E. H. Quimby for her invaluable help in the preparation of the manuscript.

Argonne National Laboratory  
P. O. Box 5207  
Chicago 80, Ill.

#### REFERENCES

- MARINELLI, L. D., TRUNNELL, J. B., HILL, R. F., AND FOOTE, F. W.: Factors Involved in the Experimental Therapy of Metastatic Thyroid Cancer with  $I^{131}$ . Preliminary Report. *Radiology* **51**: 553-557, 1948.
- MARINELLI, L. D., QUIMBY, E. H., AND HINE, G. J.: Dosage Determination with Radioactive Isotopes. II. Practical Considerations in Therapy and Protection. *Am. J. Roentgenol.* **59**: 260-280, 1948.
- METZGER, F., AND DEUTSCH, M.: The Disintegration Scheme of  $I^{131}$ . *Phys. Rev.* **74**: 1640-1644, 1948.
- OWEN, G. E., MOE, D., AND COOK, C. S.: Evidence for a Complex Disintegration of  $I^{131}$ . *Phys. Rev.* **74**: 1879-1880, 1948.
- KEATING, F. R., JR., WANG, J. C., LUELLEN, T. J., WILLIAMS, M. M. D., POWER, M. H., AND MCCONAHEY, W. M.: The Measurement of the Iodine-Accumulating Function of the Human Thyroid Gland. *J. Clin. Investigation* **28**: 217-227, 1949.
- MARINELLI, L. D., FOOTE, F. W., HILL, R. F., AND HOCKER, A. F.: Retention of Radioactive Iodine in Thyroid Carcinomas. Histopathologic and Radioautographic Studies. *Am. J. Roentgenol.* **58**: 17-30, 1947.
- FITZGERALD, P. J., AND FOOTE, F. W., JR.: Function of Various Types of Thyroid Carcinomas as Revealed by Radioautographic Demonstration of Radioactive Iodine ( $I^{131}$ ). *J. Clin. Endocrinol.* **9**: 1153-1170, 1949.
- SEIDLIN, S. M., OSHRY, E., AND YALOW, A. A.: Spontaneous and Experimentally Induced Uptake of Radioactive Iodine in Metastases from Thyroid Carcinoma. Preliminary Report. *J. Clin. Endocrinol.* **8**: 423-432, 1948.
- TRUNNELL, J. B.: Treatment of Human Thyroid Disease with Radioactive Iodine. *Tr. New York Acad. Sc. (Ser. II)* **2**: 195-201, 1949.
- ARIEL, I., ET AL.: Distribution of Radioactive Isotopes of Iodine in Normal Rabbits. *Am. J. Physiol.* **132**: 346-350, 1941.
- PERLMAN, I., CHAIKOFF, I. L., AND MORTON, M. E.: Radioactive Iodine as an Indicator of the Metabolism of Iodine. Turnover of Iodine in the Tissues of the Normal Animal, with Particular Reference to the Thyroid. *J. Biol. Chem.* **139**: 433-447, 1941.
- MANN, W., BALE, W. F., HODGE, H. C., AND WARREN, S. L.: Distribution in Rabbit Tissues of Intravenously Injected Iodine as Shown by the Radioisotope,  $I^{130}$ . *J. Pharmacol. & Exper. Ther.* **95**: 12-17, 1949.
- SALTER, W. T.: The Metabolic Circuit of the Thyroid Hormone. *Ann. New York Acad. Sc.* **50**: Art. 5, 358-376, 1949.
- SCHIFF, L., ET AL.: Gastric (and Salivary) Excretion of Radioiodine in Man. Preliminary Report. *J. Nat. Cancer Inst.* **7**: 349-354, 1947.
- FELLER, D. D., CHAIKOFF, I. L., TAUROG, A., AND JONES, H. B.: Changes Induced in Iodine Metabolism of the Rat by Internal Radiation of Its Thyroid, with  $I^{131}$ . *Endocrinology* **45**: 464-479, 1949.
- MCCONAHEY, W. M., KEATING, F. R., JR., AND POWER, M. H.: Behavior of Radioiodine in the Blood. *J. Clin. Investigation* **28**: 191-198, 1949.
- LUELLEN, T. J., KEATING, F. R., JR., WILLIAMS, M. M. D., BERKSON, J., POWER, M. H., AND MCCONAHEY, W. M.: Relative Measurement *in Vivo* of Accumulation of Radioiodine by the Human Thyroid Gland: Comparison with Radioactivity in Peripheral Tissues. *J. Clin. Investigation* **28**: 207-216, 1949.

#### SUMARIO

##### Dosimetría de la Radiación en el Tratamiento del Carcinoma Tiroideo Funcional con $I^{131}$

Con las técnicas aquí descritas puede calcularse la dosis de yodo radioactivo ( $I^{131}$ ) empleada en el tratamiento del carcinoma tiroideo funcional, no sólo para el tumor sino para ciertos otros órganos y para el cuerpo en conjunto. Esas técnicas exigen adaptación a casos dados, pero se han tomado en cuenta ciertas características en común. El método para calcular la dosis tumor aparece indicada para un individuo.

A base de la radioactividad descubierta en la sangre, orina, saliva y jugo gástrico, se ha hecho un cálculo tosco de las máximas dosis posibles de radiación llevadas a la sangre, riñones, boca y estómago de los enfermos sometidos a la terapéutica con  $I^{131}$ . Según se observó, se obtiene, como

promedio, una dosis total de radiación para el cuerpo de 108 roentgens equivalentes (er) con la administración de 100 milicurios de  $I^{131}$ , pero variaciones individuales pueden hacer desviar dicha cifra en un sentido u otro.

Con la misma cantidad de  $I^{131}$ , la dosis máxima media en el riñón es de 757 er; en el estómago, 771 er; en la boca, 2,020 er. Sin embargo, hay que considerar que esas tres dosis rezan con regiones muy limitadas de los órganos mencionados.

*Nota:* Roentgen equivalente (er) denota la cantidad de rayos beta que, en condiciones de equilibrio, desprende en 1.0 gramo de aire tanta energía como 1.0 roentgen de rayos gamma.

# Cephalohematoma in the Newborn<sup>1</sup>

M. D. INGRAM, JR., M.D., and W. M. HAMILTON, M.D.

Nashville, Tenn.

CEPHALOHEMATOMA in the newborn is of common occurrence. Its clinical features are well known, but the roentgenographic changes have received little study, and no reference to this common condition is found in the American radiological literature. Although the clinical diagnosis would seem to be simple, cephalohematoma has been confused with encephalocele and depressed skull fractures. The former diagnosis is usually suggested when the hematoma presents posteriorly in the mid-portion of the occipital bone. A depressed

## INCIDENCE

Sjövall (7) in 1936 reported an incidence of 0.41 per cent in a series of 171 newborn infants.

In the present study, a series of 126 cephalohematomata were observed in a total of 7,563 deliveries, an incidence of 1.66 per cent (Table II). Of the 126 cases, 58 involved the right parietal bone, 36 the left parietal bone, 17 were biparietal, and 15 were occipital in origin. None were found in the frontal or temporal bones. The greater number of cephalohematomata

TABLE I: WEIGHT GROUPING OF INFANTS WITH CEPHALOHEMATOMA AS COMPARED WITH THOSE OF NORMAL INFANTS (EXCLUDING STILLBIRTHS)

Group by Weight in Grams	No. of Total Births Grouped by Weight	Distribution by Weight of Total Births	Distribution by Weight of Births with Cephalohematoma	No. of Births with Cephalohematoma
Under 2,500	484	6.6%	0	0
2,500-3,000	1,216	16.3%	12.4%	15
3,000-3,500	2,895	38.9%	38.0%	45
3,500-4,000	2,207	29.7%	30.0%	40
4,000-4,500	539	7.2%	16.6%	22
4,500 and above	109	1.3%	3.0%	4

skull fracture is suggested by the presence of a palpable rim of calcium which is found in the early calcifying lesions. It is the purpose of this paper to present the interesting roentgen findings in cephalohematoma of the newborn and to analyze statistically the cases seen at the Vanderbilt University Hospital (Nashville, Tenn.) over a five-year period (1944-49).

One of the earliest reports on cephalohematoma was given in 1885 by John M. Keating (4), who accurately postulated that the tumefaction was due to the effusion of blood between the periosteum of the skull and the calvarium itself. Later authors have added little to his fundamental description, but have confined their writings to the incidence and clinical characteristics of the condition.

occurring in the parietal region is in accord with the previous reports on this subject (7).

## ETIOLOGY

Various factors have been suggested as causes of neonatal cephalohematoma. Chief among these is prolonged and difficult delivery. Hartley and Burnett (3) suggested that the fall in infant blood prothrombin seen on the second and third postpartum day might be a factor in the etiology. In the present series of cases, the following factors were considered: birth weight of the infant, sex of the infant, prenatal administration of vitamin K, fetal presentation, maternal parity, and instrumental delivery.

A study of the infant birth weight in this

<sup>1</sup> From the Department of Radiology, Vanderbilt University School of Medicine, Nashville, Tenn. Accepted for publication in January 1950.

TABLE II: TOTAL NUMBER OF DELIVERIES, SHOWING INCIDENCE OF CEPHALOHEMATOMA

Parity	No. of Cases	No. with Cephalohematoma
Primipara		
Forceps	2230	95
No Forceps	934	2
Total	3164	97
Multipara		
Forceps	1488	19
No Forceps	2911	10
Total	4399	29
TOTAL	7563	126

series reveals that this factor was of significance in neonatal cephalohematoma. The average weight of newborn infants at the Vanderbilt University Hospital over this period (1944-49) was 7 lb. 5 oz. The average weight of the infants with cephalohematoma was 7 lb. 12 oz. However, when the infants are grouped according to weight and compared with the grouping by weight of a similar series of normal infants, it can be seen that a significant difference exists. As shown in Table I, there is a larger percentage of infants in the higher weight classifications in the cephalohematoma group. (Note that none are in the premature group.)

The sex of the infant as a predisposing cause is also thought to be of some significance. There were 79 males and 47 females in this series. Statistically the fact that more male infants had cephalohematoma is of borderline significance. To be certain that sex is a factor, a larger series of cases is necessary.

The administration of vitamin K to the mother during labor had no effect in the prevention of neonatal cephalohematoma. The mothers of 51 per cent of the infants with cephalohematoma had received vitamin K and 49 per cent had not. This would tend to disprove the theory that hypoprothrombinemia in the newborn infant is a predisposing factor (3).

The fetal presentation was without etiologic significance. In 96 per cent of the cases the infants were in vertex presentation, and in 4 per cent were in breech.

These percentages are comparable to the ratio of breech to vertex presentation in normal deliveries.

Maternal parity and the use of forceps in delivery are the most interesting of all the considerations. These factors are considered together because they are fundamentally interrelated. It has been the practice at the Vanderbilt University Hospital to use episiotomy with low forceps in most of the primiparous deliveries. Table II gives a summary of 7,563 births at the Vanderbilt University Hospital and shows the number of cephalohematoma occurring in primiparous and multiparous deliveries. These are further broken down in their classification as to the use of forceps. Table III shows the incidence per

TABLE III: INCIDENCE OF CEPHALOHEMATOMA PER 1,000 DELIVERIES

	Forceps	No Forceps
Primiparae	42.6	2.1
Multiparae	12.8	3.4

1,000 deliveries of cephalohematoma in this same series. From these two tables the following conclusions can be drawn: Among the deliveries by forceps the incidence of cephalohematoma was higher in the children of primiparous than of multiparous mothers. Among the deliveries without forceps the difference in the incidence of cephalohematoma between the two groups is not significant. For both primiparae and multiparae the incidence of cephalohematoma was significantly higher in deliveries by forceps.

#### DIFFERENTIAL DIAGNOSIS

Cephalohematoma must be considered in the presence of any soft-tissue tumefaction of the skull in the newborn infant. Among these disorders are encephalocele, subcutaneous hematoma with depressed fracture, and caput succedaneum. Occipital encephalocele may simulate cephalohematoma closely. Confusion in diagnosis does not occur in the other bones because they are not mid-line in position. (It must be pointed out that rare instances of lateral



Figs. 1 and 2. Case I. The photograph of the infant shows a soft-tissue deformity of the occipital region. This was confused with encephalocele by the admitting physician. The film of the skull reveals the soft-tissue deformity in the occipital region with a rim of calcium in its peripheral portion.

encephalocele have been reported.) Roentgen study in encephalocele reveals a soft-tissue tumor with an osseous defect in the mid-line of the calvarium. There is no calcification in the base of the tumor such as is seen in the early calcifying hematoma. In cephalohematoma there is no osseous defect and after two or three weeks there is usually a faint rim of calcium at its base (Fig. 2). The most important thing in the differential diagnosis of cephalohematoma is the fact that its boundaries are limited by the periosteum of the individual bone involved. In the parietal region it is never seen to extend across the mid-line (Fig. 6). The diagnosis of depressed fracture should offer no difficulty after roentgen study. Caput succedaneum is mentioned only because reference has been made to it in earlier reports. It is, of course, a subcutaneous edema of the presenting soft part and quickly subsides following delivery.

#### PRESENTATION OF CASES

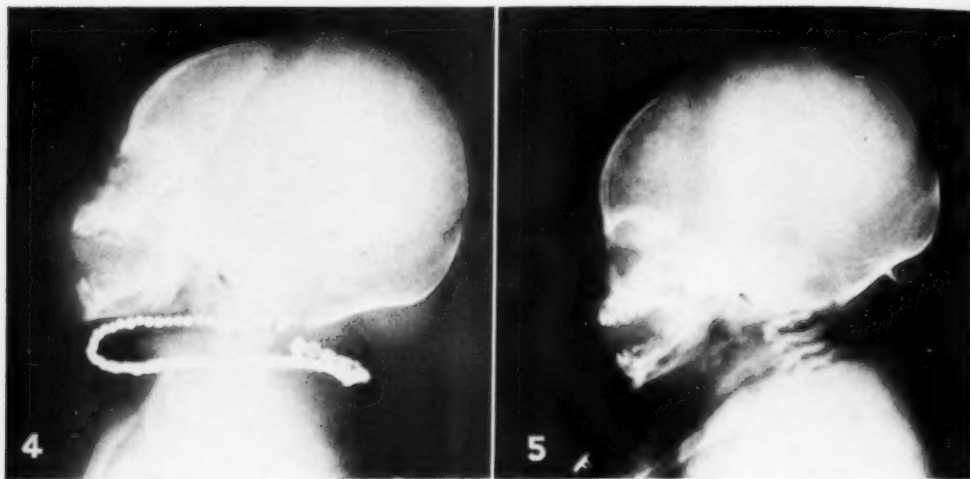
CASE I: A female infant was admitted for the first time to the Vanderbilt University Hospital at the age of four weeks. She was born by breech presentation after a difficult labor. The birth weight was 8 lb. 5 oz. A "hump" was noted on the occiput immediately after birth. On admission to this hospital physical examination revealed a spherical mass in the occipital region measuring  $7 \times 5$  cm. (Fig. 1). At its base a bony ridge could be palpated.



Fig. 3. Case II. Film of skull showing air in the subdural space with definite tumefaction in the right parietal region. This soft-tissue mass contains a thin rim of calcium at its periphery.

It was the impression of the admitting physician that the mass was an occipital encephalocele.

*Roentgen Study.* Films of the skull showed the bones of the calvarium to be normal except in the lower squamous portion of the occipital bone, where there was a spherical soft-tissue mass measuring  $5 \times 4$  cm. (Fig. 2). There was a thin layer of calcium at the base of this tumor continuous with the outer



Figs. 4 and 5. Case III. Figure 4 is a film made at the age of one week, showing soft-tissue swelling in the occipital region, without calcification. This was thought by the neurosurgeon to be an encephalocele. The film made at three weeks of age (Fig. 5) shows a thin layer of calcium at the periphery of the mass.

table of the calvarium. *Impression:* Calcifying cephalohematoma.

The mass was explored and the blood clot evacuated. The postoperative course was uneventful.

**CASE II:** A nine-weeks-old infant was admitted for the first time to the Vanderbilt University Hospital. Birth had been by low forceps. Shortly after delivery a small fluctuant tumor was found in the right parietal area. The physical examination on admission was negative except for a fluctuant mass over the right parietal bone.

*Roentgen Study:* Films of the skull revealed a soft-tissue tumor in the right parietal area, containing a thin shell of calcium continuous at its base with the outer table of the skull. Coincident spinal air studies showed subdural air beneath the hematoma (Fig. 3).

**CASE III:** A male infant was delivered at the Vanderbilt University Hospital of a primiparous mother by episiotomy and low forceps. Birth weight was 8 lb. 8 oz. At birth a soft, fluctuant mass was noted in the mid-occipital region. On clinical examination one week following delivery, it was the impression of the neurosurgeon that this was an encephalocele.

*Roentgen Study:* At one week of age, a film of the skull (Fig. 4) showed a soft-tissue tumor in the occipital region. The bones of the calvarium were not remarkable. Repeat x-ray examination at the age of three weeks (Fig. 5) showed a rim of calcium around the base of the tumor. A diagnosis of partially calcified cephalohematoma was made. No therapy was given.

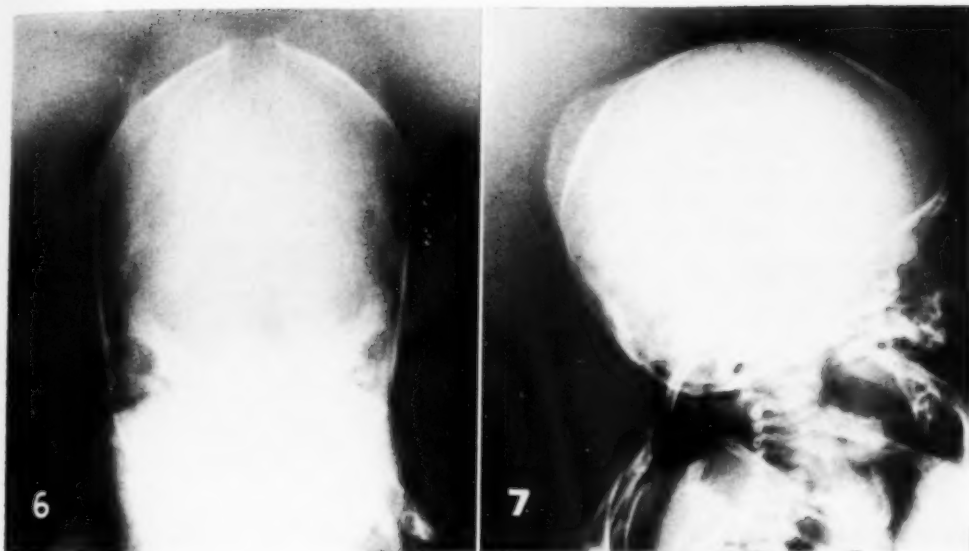
**CASE IV:** A male infant was born at the Vanderbilt University Hospital following a difficult delivery by mid-forceps. Birth weight was 8 lb. 5 oz. Bi-

lateral parietal cephalohematoma were noted at birth.

*Roentgen Study:* Films of the skull showed bilateral soft-tissue tumors in both parietal regions (Fig. 6). Films made one month later showed calcification in this area, having a laminated appearance, over the parietal bone (Fig. 7). No therapy was given. Recovery was uneventful.

#### SUMMARY

A statistical analysis of 126 cases of neonatal cephalohematoma has been presented. The incidence rate at the Vanderbilt University Hospital over a five-year period was 1.66 per cent in a total of 7,563 deliveries. It is concluded that the incidence of cephalohematoma is significantly higher when delivery is by forceps than in non-instrumental delivery. It is also shown that the birth weight of infants suffering from cephalohematoma is significantly higher than that of normal infants. Four typical cases of calcifying cephalohematoma in the newborn have been presented in detail. The clinical features of cephalohematoma have been discussed. In conclusion, it is thought that careful clinical and roentgen study will eliminate the diagnostic difficulties which have previously been encountered in cephalohematoma in the newborn.



Figs. 6 and 7. Case IV. Figure 6, an occipital view of the skull, shows soft-tissue deformity. Note that these soft-tissue swellings are sharply limited to the parietal bones bilaterally. They do not extend across the mid-line. Figure 7, four weeks later, shows definite calcification at the periphery of the soft-tissue deformity.

NOTE: Grateful acknowledgment is made to Dr. Margaret Martin, Assistant Professor of Preventive Medicine and Public Health, Vanderbilt University School of Medicine, for her gracious assistance in the preparation of the statistical data.

Vanderbilt University Hospital  
Nashville 4, Tenn.

#### REFERENCES

1. CHOROBSKI, J., AND DAVIS, L.: Cyst Formations of the Skull. *Surg., Gynec. & Obst.* 58: 12-31, January 1934.
2. COHEN, S. M., MILLER, B. W., AND ORRIS, H. W.: Meningitis Complicating Cephalohematoma. *J. Pediat.* 30: 327-329, March 1947.
3. HARTLEY, J. B., AND BURNETT, C. W. F.: An Enquiry into the Causation and Characteristics of Cephalohæmatoma. *Brit. J. Radiol.* 17: 33-41, February 1944.
4. KEATING, J. M.: Cephalohematoma—Bronchitis in Children. *Arch. Pediat.* 61: 532-540, October 1944. [Reprint 1885]
5. MORGAN, J. E.: Calcification in Cephalohematoma of the Newborn Infant. *Am. J. Obst. & Gynec.* 48: 702-705, November 1944.
6. SCHÜLLER, A.: Frontal Cephalohæmatoma. *Brit. J. Radiol.* 13: 218-219, June 1940.
7. SJÖVALL, A.: Le céphalématome des nouveau-nés. Etude d'ensemble fondée sur l'observation de 171 cas, recueillis à la maternité de Lund. *Acta obst. et gynec. Scandinav.* 15: 443-474, 1936.
8. TOOHEY, M.: Vitamin K Requirements of the Newborn. *Arch. Dis. Childhood* 17: 187-190, December 1942.

#### SUMARIO

##### Cefalohematoma en el Recién Nacido

Este estudio comprende una serie de 126 casos de cefalohematoma neonatal, representando una incidencia de 1.66 por ciento en un total de 7,563 partos. Observóse que la incidencia del estado era significativamente mayor entre los partos con fórceps que entre los no quirúrgicos. También se notó que el peso de las criaturas con cefalohematoma era significativamente más alto que el de las normales.

Al presentar 4 casos típicos, discútese las características clínicas y roentgenológicas. Roentgenológicamente, no existe deformación ósea y al cabo de dos o tres semanas ya se nota un tenue borde de calcificación en la base de la masa de tejido blando. La más importante característica diferencial consiste en que los límites de la lesión se hallan demarcados por el periostio del hueso afectado.

# Roentgen Diagnosis of Lipoma of the Corpus Callosum

## Report of a Case<sup>1</sup>

WYLIE H. MULLEN, JR., M.D., AND JOHN R. HANNAN, M.D.<sup>2</sup>

**L**IPOMA OF THE corpus callosum is a rare intracranial tumor. Rokitsansky (1) first called attention to this lesion in 1856. In 1946 List, Holt, and Everett (2) reported 2 cases and found 28 others in the world literature. A case published by Merkel (3) and one seen by Sosman (reported by Dyke, 4) were not included in their review. Sosman (6) has seen, but not reported, 4 other intracranial lipomas, 3 of which were in the mid-line. A further case has been recorded by Amyot (5). The addition of our case brings the total number of reported lipomas of the corpus callosum to 34.<sup>3</sup> Since 37 of approximately 110 verified intracranial lipomas have involved the corpus callosum, it is evident that this structure is a common location for this rather rare intracranial tumor.

### CASE REPORT

A 30-month-old white boy was first seen at the Cleveland Clinic on June 15, 1947. He was born on Dec. 30, 1944, following an eight-month pregnancy and seven hours of labor. No instruments were used. The child was apparently well until the age of six weeks, when generalized convulsions occurred, lasting fifteen to twenty minutes. Following the convulsions he appeared drowsy. Similar episodes recurred on an average of once a day until the child was nine months old. He then had attacks during which he displayed a "crooked smile" and had left facial weakness, followed by flexion and twitching movements of both arms. These episodes lasted for a little over a minute, and were not associated with loss of consciousness, loss of sphincter control, or vomiting. The attacks frequently occurred in the early morning or when the child was excited. He occasionally vomited after meals, but vomiting had been infrequent since August 1946. Monosyllabic speech began at fifteen months, and walking was not well established until the age of two. The family history was non-contributory. The father, mother, and one older sister were alive and well.

The boy appeared undernourished and underdeveloped, weighing 26 pounds. His arm and chest muscles were poorly developed. Ophthalmoscopic examination was negative. Neurologic examination revealed normal movements of the extremities. The pupils were round, equal in size, and reacted to light. Biceps and patellar reflexes were present and equal bilaterally. Triceps and Achilles reflexes were bilaterally absent. No pathologic reflexes or signs were noted. No motor disturbances were present, and, as far as could be ascertained, no sensory disturbances. The gait was wide-based, with some tendency to veer to the left.

Skull roentgenograms obtained on June 15, 1947 (Fig. 1), revealed a radiolucent area, measuring  $2.5 \times 4 \times 3$  cm., slightly above and anterior to the mid-point of the cranial vault. This area was best demonstrated on the lateral film, on which it appeared as roughly oval in shape, with a concave inferior margin. Adjacent to the upper margin a few faint calcific densities could be seen. On the postero-anterior film (Fig. 1), the radiolucent area was in the mid-line and was surrounded by faint bilateral concentric calcific lines. A diagnosis of a lipoma or intracranial dermoid tumor containing fat was suggested.

Tridione medication was instituted and the patient was sent home. He returned in one month unimproved. His attacks had continued unchanged and he had experienced frequent vomiting. Since it was believed that the vomiting might be related to the tridione, this was discontinued and phenobarbital substituted. Following the change of medication, vomiting ceased. The convulsions abated. The child continued, however, to be a "behavior problem," displaying fits of anger and discontentment two or three times a day. During these attacks he was violent, bit his mother, hit his head on the floor, and screamed.

The patient was admitted to the Cleveland Clinic Hospital on Aug. 3, 1947. On Aug. 4, encephalography was performed. The initial pressure was slightly increased. Two hundred and three cubic centimeters of clear colorless cerebrospinal fluid was removed and 213 c.c. of air injected. Laboratory examination of the fluid revealed 2 cells, no globulin, total protein 33 mg. per 100 c.c., negative Wassermann, Kahn, and colloidal gold reactions. The encephalogram (Fig.

<sup>1</sup> From the Cleveland Clinic and the Frank E. Bunts Educational Institute. Accepted for publication in January 1950.

<sup>2</sup> Now of 10515 Carnegie Avenue, Cleveland, Ohio.

<sup>3</sup> Since this paper was completed, an additional case, with roentgen studies, has been reported (D. Sutton: Radiological Diagnosis of Lipoma of the Corpus Callosum. *Brit. J. Radiol.* 22: 534, 1949).

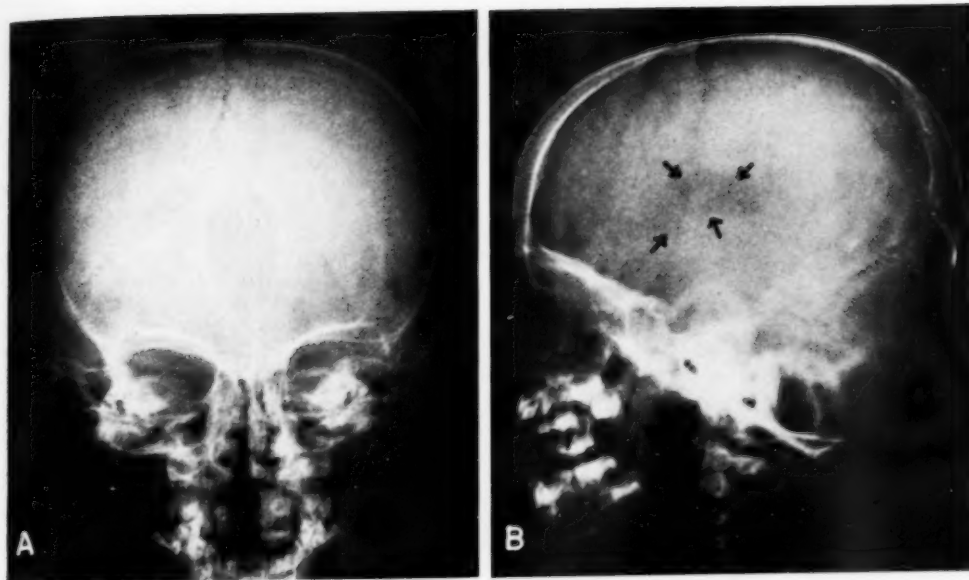


Fig. 1. Lipoma of corpus callosum: plain roentgenograms of skull. A. Postero-anterior view showing mid-line radiolucent area outlined by thin lines of calcification. B. Lateral view revealing ovoid radiolucent area. (On original films several small flecks of calcification were visible.)

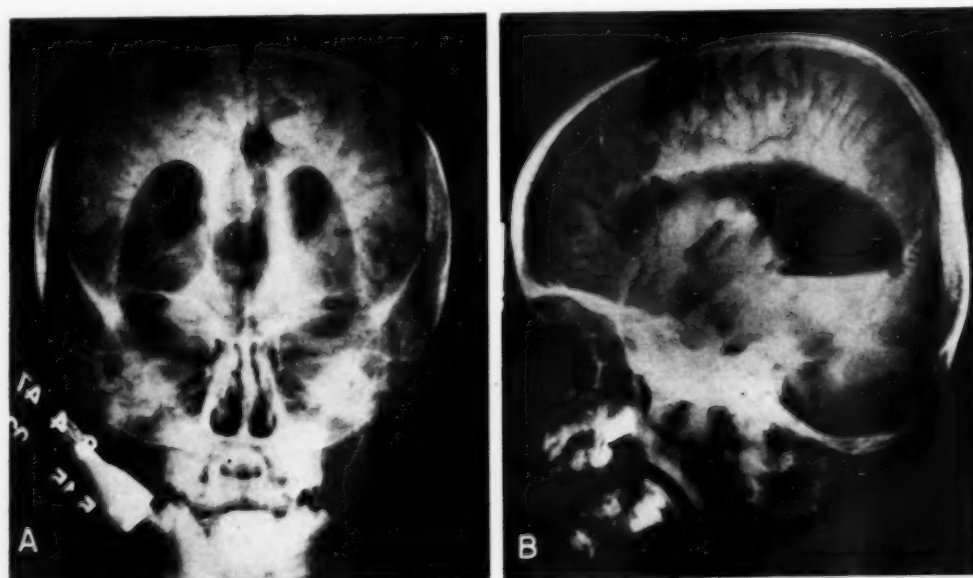


Fig. 2. Lipoma of corpus callosum: encephalographic studies. A. Antero-posterior view showing dilatation of lateral ventricles with separation of anterior horns and bodies of lateral ventricles by mid-line tumor. The medial borders of the lateral ventricles are flattened, with slight concavity. There is dilatation of the third ventricle without elevation. B. Lateral view showing marked dilatation of posterior horns and pressure deformity of anterior portions of ventricles.

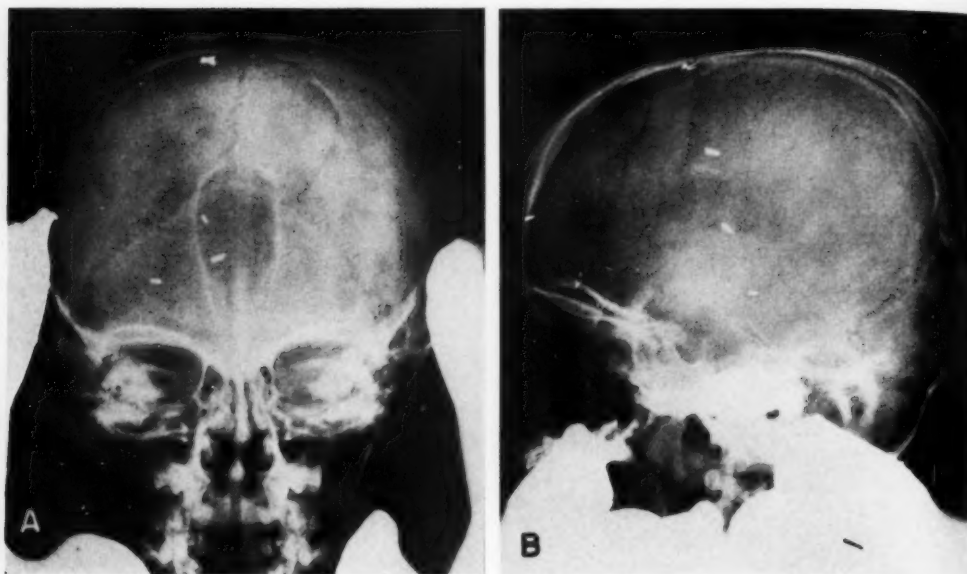


Fig. 3. Lipoma of corpus callosum: two-year follow-up film showing no essential change.

2) showed pronounced dilatation of both lateral ventricles, which were separated from each other by the radiolucent mass seen on the plain films. The medial borders of the lateral ventricles were concave. The third ventricle was dilated and appeared to be displaced posteriorly. The fourth ventricle was visible and appeared dilated. The cortical sulci, especially over the left hemisphere, were exaggerated. The roentgen diagnosis was intracranial lipoma arising in the region of the corpus callosum.

On Aug. 8, 1947, a midfrontal craniotomy was performed by Dr. W. James Gardner, and a biopsy specimen was obtained of a lipoma of the anterior genu of the corpus callosum. Under avertin-ether anesthesia, with the patient in the supine position, a craniotomy was performed with the craniotome. The posterior border of the opening was at the coronal suture. The dura on the right side of the sagittal sinus was incised, and, after division of one cerebral vein, the frontal lobe was retracted from the falx. The mesial surface of the right frontal lobe was extraordinarily vascular, with large tortuous arteries and veins suggesting a cirroid aneurysm. Because of the extreme vascularity, it was decided to attempt an intraventricular exposure of the mass. Accordingly, an incision was made through the cortex to the right of the sagittal sinus and was carried downward into the anterior horn of the ventricle. Lighted retractors were introduced and a pedunculated tumor could be seen, perhaps  $1.0 \times 0.5$  cm. in diameter, lying near the foramen of Monro. This was picked up and after division of the attached choroid plexus the

tumor was removed. The mass which had been disclosed roentgenographically caused a swelling on the mesial surface of the ventricle just above and in front of the foramen of Monro. Here a firm tumor was visible and palpable beneath the lining of the ventricle. Some tissue was removed for microscopic study. An attempt was again made to expose the tumor by the extracerebral route. The frontal lobe was retracted once more, some additional vessels running to the falx were divided, and what had first been taken for the anterior genu of the corpus callosum was found to be a firm, yellowish, fatty tumor containing some calcium. An incision was made into the mass and some tissue removed for microscopic study. After careful inspection and consideration, it was finally deemed inadvisable to attempt to remove the lesion. The dura was closed. Bleeding points on its outer surface were controlled with Gelfoam soaked in thrombin solution. The section of bone was replaced and the scalp closed with a single buried tier of interrupted black silk sutures.

One specimen consisted of a firm, round encapsulated, bright yellow tumor measuring 1 cm. in diameter with attached choroid plexus. There were, in addition, a few small fragments of firm, yellowish-white tissue which had been removed from the encapsulated mass above the corpus callosum. Microscopically the yellow mass in the choroid was formed by typical adult fat tissue, finely trabeculated with connective tissue. A section from the mass above the corpus callosum showed portions of brain tissue, and one fragment of fat tissue of the adult type.

The patient had a stormy postoperative course with convulsions, mostly left-sided, lasting twenty to thirty minutes. There was fever up to 104° F. with associated meningeal signs. Left-sided jacksonian convulsions continued and required large doses of barbiturates for control. Lumbar puncture, on Aug. 16, revealed an initial pressure of 140 mm. with normal pulsations. Two cubic centimeters of clear yellow fluid was removed. The cell count was 400, with only 70 white blood cells. Culture revealed *Staphylococcus albus*. Fifteen thousand units of penicillin were given intramuscularly every three hours and continued until 480,000 units had been given. On Aug. 20, temperature became normal, and remained so until discharge on Aug. 22.

Since discharge the patient has been observed at the Cleveland Clinic on numerous occasions. His last visit was on June 23, 1949. He has had almost no seizures for the last one and one-half years, dilantin, gr. 1/2 twice a day, and phenobarbital, gr. 1/2 four times a day, having been prescribed. He has, however, remained a behavior problem, requiring much attention and displaying frequent temper tantrums. He has developed well physically, has a good appetite, and has fairly good bowel and bladder control. His memory and speech have improved but are still below normal for a boy his age. Physical examination is essentially negative except for a slight tendency toward internal squint.

Films taken on May 23, 1949, reveal the previously described radiolucent area, unchanged from the original examination except for a questionable increase in calcification (Fig. 3).

**Comment:** To our knowledge this is the first lipoma of the corpus callosum surgically verified but not excised. The two-year clinical and roentgenologic follow-up studies substantiate the assumption that these lesions are slow-growing. Our case is the sixth to be reported in which plain roentgenograms were obtained, and the fourth with air studies. This case and that of Amyot reveal the encephalographic findings in lipomas of the corpus callosum without associated agenesis of the corpus callosum. The cases of List, Holt and Everett (2) and of Sosman (4) had an associated agenesis of the corpus callosum.

#### ETIOLOGY

The etiology of this tumor is at the present time unknown. For a detailed discussion of the pathogenesis of intracranial lipomas, the reader is referred to

the excellent papers of Krainer (7), List, Holt, and Everett (2), Merkel (3), and Vonderahe and Niemer (8).

#### PATHOLOGY

In all the reported cases of lipoma of the corpus callosum the tumors have been situated on the dorsal surface, closely following the superior contour of the structure. Although they usually cover only the anterior part of the corpus callosum, they may cover it all or only the posterior part. The reported lipomas have varied in size from a few millimeters to tumors as large as 5 or 6 cm. in diameter. As in our case and several others (de Steiger, 9; Bartel, 10; Kirkbride, 11; Abrikossow, 12; Rubinstein, 13; Merkel, 3; List, Holt, and Everett, 2; Gander, 14), additional separate lipomas may be present in the choroid plexuses. They have been seen in other localities less frequently.

The tumor is usually well demarcated from the surrounding brain tissue. However, in Huddleson's case (15) the growth appeared to invade contiguous tissue and in Merkel's case it was poorly demarcated inferiorly and extended throughout the entire thickness of the corpus callosum. The pia arachnoid of the sulcus of the corpus callosum seems to form the capsule for the underlying tumor; for this reason the anterior cerebral arteries usually traverse the tumor or its covering. As viewed laterally, the lipoma may be flat, streak-like, or generally ovoid, with a concave undersurface. Calcification is nearly always present in the periphery, in the capsule, or in the adjacent brain tissue. Actual ossification has been reported in a few cases.

The microscopic picture is identical with that of lipoma found in other locations, showing mature fat cells, fibrous tissue, and occasional calcium deposits. The tumor is always benign. Cerebral lipomas do not contain dermal structures or neural tissue (7).

Various associated brain anomalies have been reported, the most common of which is complete or partial absence of the corpus

callosum. Sosman (16) in 1946 stated that all 3 confirmed cases of lipoma of the corpus callosum which he had seen had had an associated agenesis of the corpus callosum. He thought that a mid-line lipoma of the brain was generally accompanied by agenesis of the corpus callosum. However, as pointed out by List, Holt, and Everett, these lesions are not always coexistent. Among the 34 reported cases, varying degrees of agenesis have been found in 13 (2, 4, 11, 13, 15, 17-23). In 1932, Baker and Graves (24) collected from the literature and reviewed 82 autopsied cases of partial agenesis of the corpus callosum in which there was no accompanying lipoma. Bunts and Chaffee (25) found, in 1944, 15 cases (including 1 of their own) of agenesis of the corpus callosum diagnosed by encephalography; they did not report a single associated lipoma.

#### CLINICAL FINDINGS

The clinical picture is variable, ranging from complete lack of symptoms in the small tumors to mental change, jacksonian or generalized convulsions, and hemiparesis in patients with larger tumors. There is no sex preference. It is practically impossible to make a positive diagnosis of lipoma of the corpus callosum from the clinical findings alone. Agenesis of the corpus callosum, as well as other mid-line anomalies (without an associated lipoma), can produce the same picture (25, 26). The clinical signs of increased intracranial pressure are usually absent. The tumor has been discovered in all decades up to and including the seventh. The youngest reported patient was three days old (second case of List, Holt, and Everett) and the oldest was seventy-five years of age (Fattovich, 27).

#### ROENTGENOLOGIC CONSIDERATIONS

Sosman (4) was given credit in 1939 for the first accurate roentgenologic diagnosis of lipoma of the corpus callosum. Because of the relative radiolucency of fat tissue as compared to the normal density of brain tissue, a lipoma of any

size will be recorded on the roentgenograms as an area of decreased density. This finding is pathognomonic for fat tissue. The mid-line location of the area of decreased density above or in the normal location of the corpus callosum is essential for the diagnosis of lipoma. The radiolucent area is more readily visualized in lateral views than in sagittal views. The superimposition of frontal sinuses, the greater depth of the brain, and the thick posterior skull wall in the sagittal projection may explain this. If the tumor is small or if the skull films are improperly exposed, this area of increased density may be overlooked.

Calcification is frequently present in the periphery of the lipoma, varying from an amount barely visible roentgenologically to densities resembling bone. In the sagittal projection, the calcification is usually visualized as two fairly dense curvilinear deposits surrounding the area of decreased density. The shadows lie to either side of the midline, and are convex laterally. In our case, as in the first case of List, Holt, and Everett, and in the case of Amyot, this calcification was more easily identified in the sagittal projections than in the coronal projections. On the lateral film in the case of List, Holt, and Everett, the calcification was not recognized, and in our case it was only faintly perceptible as a few scattered densities along the upper contour of the radiolucent shadow. The explanation for this may be that the calcification exists in relatively thin long sheets in or along the tumor capsule. As in somewhat similar deposits in the falx, the calcification is demonstrated more easily on sagittal roentgenograms of the skull.

The roentgen signs of increased intracranial pressure, often seen with other brain tumors, are not observed in lipomas of the corpus callosum. Diagrammatic reproduction of the plain skull films of the reported cases having roentgenograms are seen in Figure 4.

The cases of Sosman, Amyot, List, Holt, and Everett, and our own case are

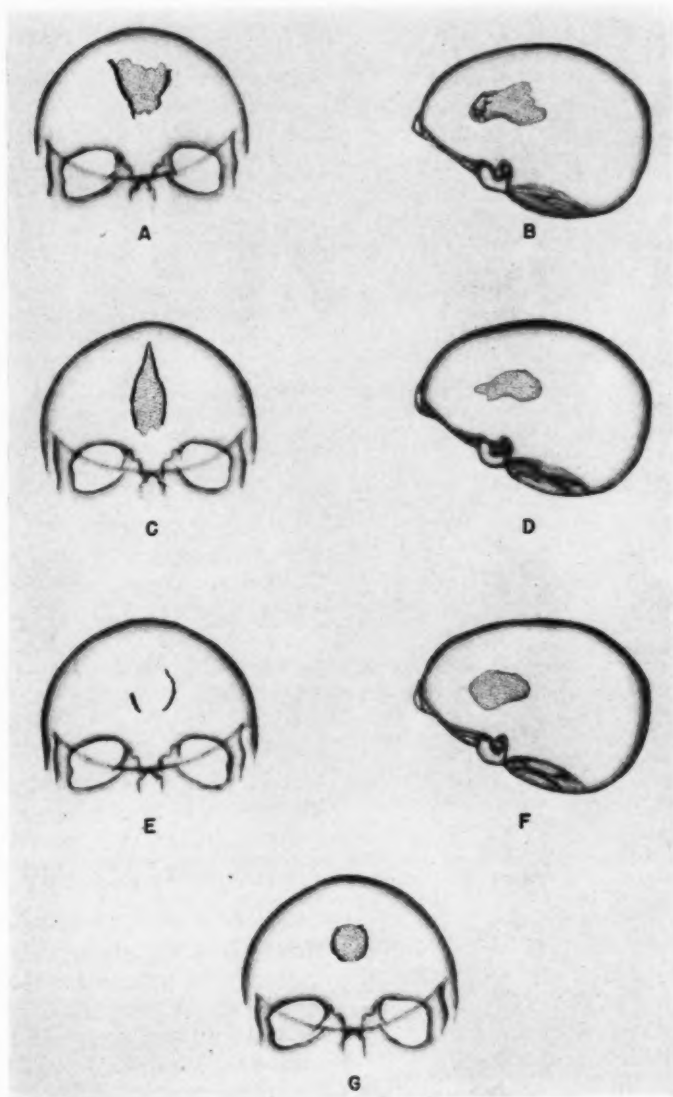


Fig. 4. Diagram of plain films of reported cases of lipoma of corpus callosum. A and B (Sosman, reported by Dyke): Radiolucent area and calcification visible on both postero-anterior and lateral films. C and D (Ehni and Adson): Calcification apparent on postero-anterior view only. Second case of Ehni and Adson not shown because roentgenograms were considered normal. E and F (List, Holt, and Everett): Calcification demonstrated on postero-anterior film only. Radiolucent area visible on lateral film only. G (Amyot): Postero-anterior view revealing calcification and radiolucent area. (Dark lines represent calcification. Stippled areas represent radiolucent tumors.)

apparently the only ones having had air studies. These cases have all shown the following constant changes: (1) the portions of the lateral ventricles adjacent to

the tumor are separated; (2) the lateral ventricles are dilated; (3) the mesial borders of the lateral ventricles adjacent to the tumor are concave. Of these

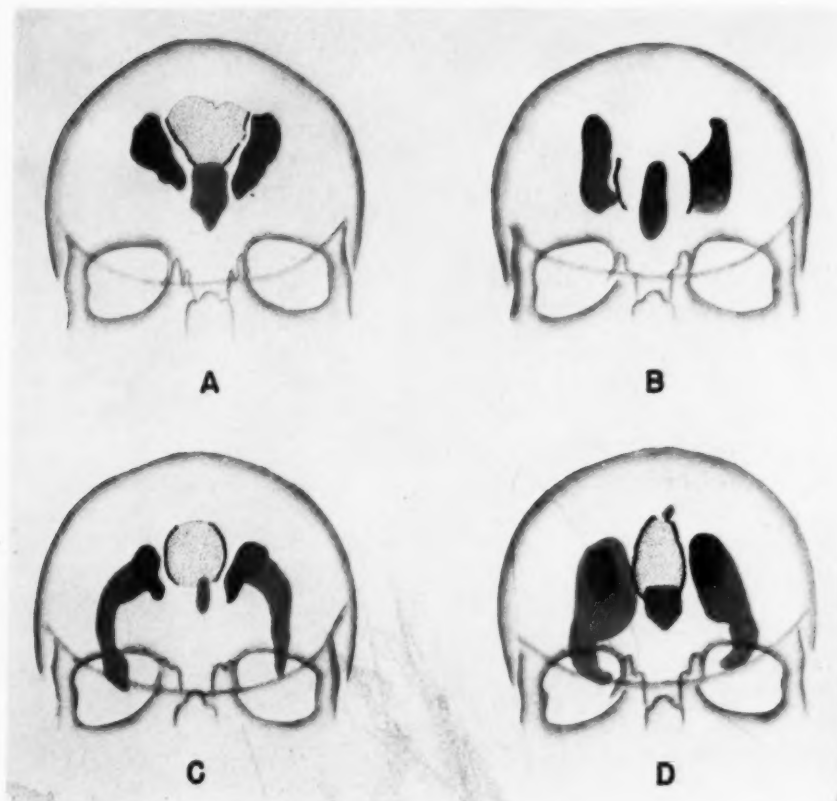


Fig. 5. Air-studies. A (Sosman, reported by Dyke): Lipoma of corpus callosum with associated agenesis of corpus callosum. B (List, Holt, and Everett): Lipoma with associated agenesis of corpus callosum. C (Amyot): Lipoma of corpus callosum without agenesis. D (Mullen and Hannan): Lipoma without agenesis of corpus callosum.

findings, the most constant and probably most diagnostic sign is the separation of the lateral ventricles, especially if a radio-lucent mass partially circumscribed by calcium is seen lying between them.

The variation in air studies depends chiefly on whether or not there is agenesis of the corpus callosum. Davidoff and Dyke (28), in 1934, described the following encephalographic findings in that condition: (1) marked separation of the lateral ventricles; (2) angular dorsal margins of the lateral ventricles; (3) concave mesial borders of the lateral ventricles; (4) dilatation of the caudal portions of the lateral ventricles; (5) elongation of the interventricular foramina; (6) dorsal extension and dilatation of the third ven-

tricle; (7) radial arrangement of the mesial cerebral sulci around the roof of the third ventricle and extension of the sulci through the zone usually occupied by the corpus callosum. Bunts and Chaffee, reviewing the encephalographic findings of 15 cases of agenesis of the corpus callosum, noted considerable variation in size and shape of the lateral ventricles. They found that pointed dorsal margins of the lateral ventricles were not consistently present.

As previously stated, the lipomas seen by List, Holt, and Everett and by Sosman were associated with agenesis of the corpus callosum. In the case of List, Holt, and Everett, the ventriculograms suggested that the anterior portions of the lateral ventricles were spread by a mid-

line mass, the periphery of which was partially outlined by calcification. The posterior portions of the lateral ventricles were moderately dilated, and the slightly enlarged third ventricle was elevated. In Sosman's case, there was separation of the lateral ventricles and flattening of the third ventricle; in addition, the third ventricle appeared slightly elevated. In Amyot's case and in our own the corpus callosum was intact and consequently there was no elevation of the third ventricle nor flattening of its roof. It thus appears that a lipoma associated with agenesis of the corpus callosum will show, in addition to the constant findings previously listed: (1) angular dorsal margins of the lateral ventricles; (2) some elevation of the third ventricle (the lipoma prevents elevation to the pronounced extent seen in agenesis alone); (3) flattening of the superior surface of the third ventricle by the tumor.

If the tumor is small and streak-like, and the corpus callosum is present, it is reasonable to assume that the encephalogram might be normal or might show so little change as to be non-diagnostic.

Diagrammatic representations of the air studies of the reported cases of lipoma of the corpus callosum are shown in Figure 5.

#### DIFFERENTIAL DIAGNOSIS

Gliomas of the corpus callosum may show calcification, but the calcification does not have the dense linear character or the peripheral distribution seen with lipomas. The pathognomonic radiolucent area is not present in this group of tumors.

Bunts and Chaffee feel that a communicating cyst of the cavum septi pellucidi is the only lesion which could be confused with agenesis of the corpus callosum. This lesion is not likely to be confused with a lipoma of the corpus callosum because cysts of the cavum septi pellucidi do not contain calcium nor do they produce radiolucent areas on plain skull films.

Tumors of the septum pellucidum, non-communicating cysts of the septum pellucidum, and ependymomas arising in the me-

dial wall of the lateral ventricles may similarly separate the lateral ventricles. None of these lesions, however, show the typical peripheral calcification or pathognomonic zone of decreased density.

A large calcified suprasellar cyst can be differentiated from a lipoma, since suprasellar cysts do not produce radiolucent areas on the plain films and the encephalographic changes differ noticeably from those due to lipoma. Craniopharyngiomas are in closer approximation to the sella turcica, and often produce erosion of this structure.

#### SURGICAL CONSIDERATIONS

To date the results following attempted excision of a lipoma of the corpus callosum have been discouraging. Ehni's and Adson's (23) patient died a few days post-operatively. The patient of List, Holt, and Everett became a hopeless "brain cripple" and died five months later. Amyot's patient deteriorated greatly following surgical removal of the lipoma. As pointed out by List, Holt, and Everett, the technical factors involved in the removal of a mass the size of a hen's egg from the surface of the corpus callosum are not hazardous. The frequent inclusion of both anterior cerebral arteries within the body or the coverings of the tumor is the almost unsurmountable obstacle. Complete removal of the lipoma without damage to one or both of these important vessels is technically almost impossible. Although it has not yet been reported, it is reasonable to assume that cerebral angiography would reveal the relationship of the anterior cerebral vessels to the tumor.

It is generally agreed that excision of a lipoma of the corpus callosum is contraindicated. It is therefore the responsibility of the roentgenologist and the neurosurgeon to diagnose this lesion without surgical exploration.

#### SUMMARY

A case of lipoma of the corpus callosum, surgically verified but not completely

removed, is presented. It is believed to be the sixth reported case in which plain roentgenograms of the skull were obtained, and the fourth to be studied encephalographically.

In nearly all cases the diagnosis can be established by the pathognomonic findings revealed in the plain skull films. Air studies are not essential, but may add considerable information concerning the presence or absence of the corpus callosum.

Cleveland Clinic  
Cleveland 6, Ohio

#### REFERENCES

1. ROKITANSKY, C.: Cited by List, Holt, and Everett (2).
2. LIST, C. F., HOLT, J. F., AND EVERETT, M.: Lipoma of Corpus Callosum; Clinicopathologic Study. *Am. J. Roentgenol.* **55**: 125-134, February 1946.
3. MERKEL, H.: Zur Frage der Balkenlipome. Zugleich ein Beitrag zur Entwicklungsgeschichte des Balkens. *Ztschr. f. d. ges. Neurol. u. Psychiat.* **171**: 269-277, 1941.
4. DYKE, C. G.: Roentgen-Ray Diagnosis of Diseases of the Skull and Intracranial Contents. In *Diagnostic Roentgenology*, Golden, R., editor, New York, Thomas Nelson & Sons, 1947, Vol. 1, Chap. I, pp. 33 F-G-H.
5. AMYOT, R.: Contribution à l'étude du lipome du corps calleux. *Union méd. du Canada* **75**: 1391-1406, November 1946.
6. SOSMAN, M. C.: Personal communication.
7. KRÄINER, L.: Die Hirn- und Rückenmarkslipome. *Virchows Arch. f. path. Anat.* **295**: 107-142, 1935.
8. VONDERAHE, A. R., AND NIEMER, W. T.: Intracranial Lipoma; Report of Four cases. *J. Neuropath. & Exper. Neurol.* **3**: 344-354, October 1944.
9. DE STEIGER, A.: Two Cases of Lipoma of Brain. *J. Ment. Sc.* **48**: 64-66, January 1902.
10. BARTEL, J.: Cited by Krainer (7).
11. KIRKBRIDE, T.: Lipoma of Brain. *Path.-Anat. Arb. Joh. Orth. z. Prof. . . . Jubil.*, pp. 515-519, 1903.
12. ABRIKOSOW, A.: Cited by List, Holt, and Everett (2).
13. RUBINSTEIN, B. G.: Cited by List, Holt, and Everett (2).
14. GANDER, G.: Un cas de lipome du corps calleux. *Ann. d'anat. path.* **14**: 513-520, June 1937.
15. HUDDLESON, J. H.: Ein Fall von Balkenmangel mit Lipomentwicklung im Defekt. *Ztschr. f. d. ges. Neurol. u. Psychiat.* **113**: 177-192, 1928.
16. SOSMAN, M. C.: In discussion of paper by Echternacht and Campbell (26).
17. BENJAMIN, L.: Cited by List, Holt, and Everett (2).
18. WÜRTH, A.: Cited by List, Holt, and Everett (2).
19. ERNST, P.: Cited by Krainer (7).
20. VON SURY, K.: Ein gemischtes Lipom auf der Oberfläche des hypoplastischen Balkens. *Frankfurt. Ztschr. f. Path.* **1**: 484-491, 1907.
21. HUEBSCHMANN: Cited by Krainer (7).
22. JUBA, A.: Über einen mit Lipomatose verbundenen Fall von partiellem Balkenmangel. *Arch. f. Psychiat.* **106**: 324-332, 1937.
23. EHNI, G., AND ADSON, A. W.: Lipoma of Brain. Report of Cases. *Arch. Neurol. & Psychiat.* **53**: 299-304, April 1945.
24. BAKER, R. C., AND GRAVES, G. O.: Partial Agenesis of Corpus Callosum. *Arch. Neurol. & Psychiat.* **29**: 1054-1065, May 1933.
25. BUNTS, A. T., AND CHAFFER, J. S.: Agenesis of Corpus Callosum with Possible Porencephaly. Review of Literature and Report of Case. *Arch. Neurol. & Psychiat.* **51**: 35-53, January 1944.
26. ECHTERNACHT, A. P., AND CAMPBELL, J. A.: Midline Anomalies of the Brain. Their Diagnosis by Pneumoencephalography. *Radiology* **46**: 119-131, February 1946.
27. FATTOVICH, G.: Contributo allo studio dei lipomi del corpo calloso. *Riv. di pat. nerv.* **52**: 310-320, September-October 1938.
28. DAVIDOFF, L. M., AND DYKE, C. G.: Agenesis of Corpus Callosum; Its Diagnosis by Encephalography. Report of Three Cases. *Am. J. Roentgenol.* **32**: 1-10, July 1934.

#### SUMARIO

##### Diagnóstico Roentgenológico del Lipoma del Cuerpo Calloso: Observación

El caso descrito es de lipoma del cuerpo calloso, comprobado quirúrgicamente, aunque no extirpado del todo. Los roentgenogramas simples del cráneo revelaron una zona radioluciente en la línea media y débiles rayas concéntricas de calcificación, estas últimas observadas mejor en las proyecciones sagitales. La encefalografía mostró pronunciada dilatación de ambos ventrículos laterales, que estaban separados entre sí por la tumefacción radioluciente observable en la radiografía corriente. En este caso no había agenesia asociada

del cuerpo calloso, aunque la misma ha sido comunicada frecuentemente.

Por estar contraindicada la excisión en el lipoma del cuerpo calloso, hay que establecer el diagnóstico roentgenológicamente para evitar la innecesaria intervención cruenta. En casi todos los casos cabe establecer el diagnóstico por el típico aspecto en la radiografía corriente. Los estudios con aire no son indispensables, pero pueden aportar considerable información con respecto a la posible agenesia del cuerpo calloso.

## Radiographic Changes in the Lungs During Recovery from Drowning<sup>1</sup>

JEROME J. ROMAGOSA, M.D., LEON J. MENVILLE, M.D., and JOHN T. LECKERT, M.D.<sup>2</sup>

New Orleans, La.

WHILE DEATH from drowning occurs frequently, it is not uncommon for persons who have been removed from water in an unconscious state to be revived. Yet, in a review of 637,586 admissions to the Charity Hospital in New Orleans, during a twelve-year period, we were able to find only 12 instances in which the diagnosis was listed as submersion and drowning. Of these 12 patients, 9 recovered. In only one case, which we are reporting, was an x-ray examination of the chest made.

In a perusal of the English and French medical literature of the past thirty-five years, we were able to find only one report of the x-ray changes in the lungs in three human cases following drowning. This one report was published in French by Trocmé and Lafarie (1).<sup>3</sup> Sante (2), in describing the roentgenologic picture of acute and azotemic edema, says: "The picture is somewhat similar to that seen in drowning where large amounts of water fill the lung. If recovery takes place, the return of the roentgen picture to normal is equally prompt in both conditions." In a personal communication Sante (3) states: "My experience with x-ray examination of patients who have nearly drowned has been limited to those who have recovered. From those which we have seen the picture has been essentially one of acute edema of the lungs which has rapidly absorbed."

It is apparent that but few cases have been reported in which x-ray examination of the lungs of drowning persons has been made. On the other hand, the literature includes considerable experimental work on the pathology and abnormal physiology

in animals in the process of drowning. Karpovich (4) has shown that water enters the lungs of drowning animals in an amount varying from 12.5 to 36.9 c.c. per kilogram of body weight. He further states that he investigated the distribution of water in the lungs of rats drowned in a colored solution. In every case, colored water and froth were found in the trachea and bronchi, and colored areas were easily seen on the surfaces of the lungs. These colored areas were especially frequent on the lower lobes, sometimes occupying half of the mediastinal and diaphragmatic surfaces; occasionally the apices were also colored. Karpovich's observations indicate that water may reach any part of the lungs. Swann and co-workers (5) state that Cot (6) calls attention to the high protein content of the fluid found in the lungs of drowned victims and suggests that the aspirated water causes fulminating pulmonary edema and that it is the edematous fluid which "drowns" the victims.

To summarize the work of Swann and co-workers (5), with dogs, it was found that in fresh-water drowning:

- (1) Arterial blood O<sub>2</sub> dropped rapidly after the beginning of drowning and the whole blood CO<sub>2</sub> rose rapidly.
- (2) Hemodilution occurred soon after the beginning of drowning and continued rapidly for five minutes, with rapid decrease in the blood density, hemoglobin, plasma proteins and whole blood chlorides.
- (3) Systolic arterial blood pressure, but not diastolic, rose rapidly and

<sup>1</sup> From the Department of Radiology, Division of Diagnostic Roentgenology, Charity Hospital of Louisiana in New Orleans. Accepted for publication in February 1950.

<sup>2</sup> Resident in Internal Medicine, Louisiana State University, Medical Service.

<sup>3</sup> Trocmé and Lebert have more recently reported 2 additional cases with roentgen findings (*J. franç. de méd. et chir thorac.* 3: 308, 1949. *Abst. in Radiology* 55: 289, 1950).—Ed.

leveled off. At this time the pulse rate was very slow. The ventricles fibrillated 3 to 5.6 minutes after drowning began.

- (4) Throughout the period of drowning, the effective venous pressure was high. At cardiac arrest it remained high, due probably to increased blood volume.
- (5) At autopsy, the lungs, particularly in their dependent parts, were hemorrhagic, were soggy and tremendously enlarged, did not collapse spontaneously, and floated in water.

On the other hand, following sea-water drowning, the following observations were made:

- (1) Strong hemoconcentration occurred.
- (2) No ventricular fibrillation occurred.
- (3) The blood pressure was lower.
- (4) The venous pressure was sustained until cardiac failure, when it dropped to zero. This is probably due to the lowered blood volume.
- (5) Autopsy of lungs was essentially the same as in fresh-water drowning.

Jetter and Moritz (7) state that a certain movement occur in sea-water drowning in which the salts pass into the blood stream. They found large quantities of magnesium (15.3 mg. per cent) in the plasma of drowned dogs. According to Loughheed, Janes, and Hall (8), at autopsy the whole bronchial system was usually found to be filled with a frothy fluid, considered to be a mixture of aspirated water, alveolar gas, and edema fluid. Many large congested-looking areas were seen on the surfaces of the lungs. The lungs were crepitant and, in a large percentage of the cases, floated in water. Foamy fluid exuded from the cut surfaces.

It is of interest to present a brief summary of the three human cases reported by Trocmé and Lafarie.

**CASE I (Trocmé and Lafarie):** A 53-year-old sailor who had been removed in an unconscious state after submersion in water was revived by artificial respiration. Low-grade fever subsequently

developed, which lasted for five or six days, along with subcrepitant râles accompanied by coughing. An x-ray examination was first made on Aug. 7, thirty-six hours after submersion. The roentgenogram showed linear opacities extending throughout most of the lung fields. The markings are particularly accentuated in the bases and perihilar regions. The radiographic markings had the appearance of a diffuse tuberculous bronchopneumonia. The next x-ray examination was made on Aug. 9, showing resolution of the greater part of the opacities. Discrete shadows persisted in both lungs, and there was decreased translucence in the right pericardiac region. The last x-ray examination was made on Aug. 13 and showed no significant abnormality.

**CASE II (Trocmé and Lafarie):** An 18-year-old boy, on Aug. 11, was removed in an unconscious state from submersion in water and was revived after twenty minutes of artificial respiration. An x-ray examination made on Aug. 12, about twenty hours after drowning, showed more or less confluent linear opacities throughout both lung fields except in the peripheral and subclavicular regions. On Aug. 14, x-ray examination revealed considerable resolution with some remaining opacities on the left side. Another examination, made on Aug. 16, showed further resolution, with complete clearing on the left. Some perihilar opacities remained on the right. The final examination was made on Aug. 19 and demonstrated no significant abnormality.

**CASE III (Trocmé and Lafarie):** A young man drowned while swimming on Sept. 23 and was revived after half an hour by artificial respiration. On the next day a low-grade fever developed, which lasted five days. Subcrepitant râles were heard in the right base, which cleared up by the fifth day. An x-ray examination was made on Sept. 23, twenty hours after drowning, showing soft non-homogeneous opacities in the right perihilar region and similar opacities in the right pericardiac region. Subsequent x-ray examinations, made on Sept. 26, 27, and 30, revealed rapid resolution.

Trocmé and Lafarie offer the two following hypotheses in explaining their radiographic findings: (1) that they could be produced by the presence of water in the respiratory passages and alveoli, and by modifications caused by the water in the permeability of certain parts of the pulmonary tissues; (2) that they could be caused by inflammatory lesions following infection of the alveoli by bacteria in the water. They consider their first hypothesis the most plausible, since the opacities are more prominent on the first film and subside rapidly.

In order to obtain a clearer understanding

of the pathogenesis of their radiographic images, Trocmé and Lafarie experimented on drowning cats, believing that the x-ray images are sufficiently comparable to those of men. They report that immediately after drowning, before revival of the animals, bilateral strands of homogeneous opacity are visualized, often very extensive, extending even into the pulmonary apices. These opacities became more fragmented upon the return of respiration and were comparable to the opacities observed in human beings at a similar phase. Also, they disappeared progressively on the following days in a manner similar to that observed in man. The authors believed it probable that if radiographs of human subjects were made before the onset of respiration, the findings would be the same as those observed in animals.

Trocmé and Lafarie concluded from their clinical and experimental observations that the pulmonary changes observed on the roentgenograms of drowned persons may be due to mechanical causes and also to the presence of water in the bronchial system. They question whether water alone is responsible for these changes, since mechanical causes offer a more logical explanation for the presence of abnormal lung findings persisting for several days. They also have considered as a possible explanation for the lung changes segmental atelectasis produced by edema of the bronchial musculature, or even as a result of an alveolar exudate in the alveoli of certain bronchi which have been momentarily obstructed.

We are presenting our case to demonstrate the abnormal radiographic changes evident in the lungs during the course of recovery from drowning, along with a discussion of the pathogenesis of the abnormal findings.

#### CASE REPORT

The patient was a 34-year-old priest who, the morning of June 5, 1949, celebrated late Mass, which was followed by a heavy dinner. He then attended a gymnasium and received a Turkish bath, during which time he felt weak. Immediately after the bath he went in swimming and fainted a few minutes after entering the water. Following submersion,

for an unknown period, the patient was rescued and given artificial respiration by the Schäfer technic. The Charity Hospital ambulance was summoned, and oxygen was administered by a portable respirator during transportation to the hospital. On admission to the emergency room, the patient was unconscious, cyanotic, and vomiting. He was placed in the Trendelenburg position, suction was instituted, and oxygen continued. He regained consciousness shortly thereafter, was transferred to the observation ward, and given penicillin. Oxygen was discontinued the next day. The hospital course was essentially uneventful and the patient was discharged June 17, 1949.

*Roentgen Findings:* The first chest film (Fig. 1) was obtained on June 7, approximately thirty-six hours after admission. The heart and large vessels, in the erect postero-anterior view, were about normal in size, shape, and position. The hemidiaphragms were rounded and smooth. The costophrenic angles were clear. The cardiophrenic angle was obscured. The lungs showed mottled opacities, with areas of confluence in the inner two-thirds of the lung fields, in both pericardiac regions, somewhat more pronounced on the right than on the left. The peripheral lung fields appeared clear. Subsequent roentgenograms on following days demonstrated progressive clearing. At the end of the three weeks (Fig. 2) the chest showed no significant abnormality.

#### DISCUSSION

Since in our case drowning was the result of aspiration of water, it was thought to be of interest to know the content of the aspirated water, since chemicals of an irritating nature may play a part in the abnormal roentgenographic appearance of the lungs. We accordingly procured a chemical analysis of the water in some of our public and private swimming pools, which may compare with the water in swimming pools of other cities in this country. The following information was obtained from Mr. John Morrell of the New Orleans Sewerage Water Board and from Mr. Cassius Clay of the Louisiana Public Health Service:

- (1) *Audubon and City Park Pools:* These pools used chloramine, a mixture of chlorine and ammonia in the dilution of 0.7 part of chloramine to one million parts of water.
- (2) *New Orleans Athletic Club Pool:* No chloramine used. Water is obtained from a salt water well, 1,250 feet deep. The water is changed daily. Before going into the pool, the water is filtered, but this does not affect the salt content. The water in the pool has

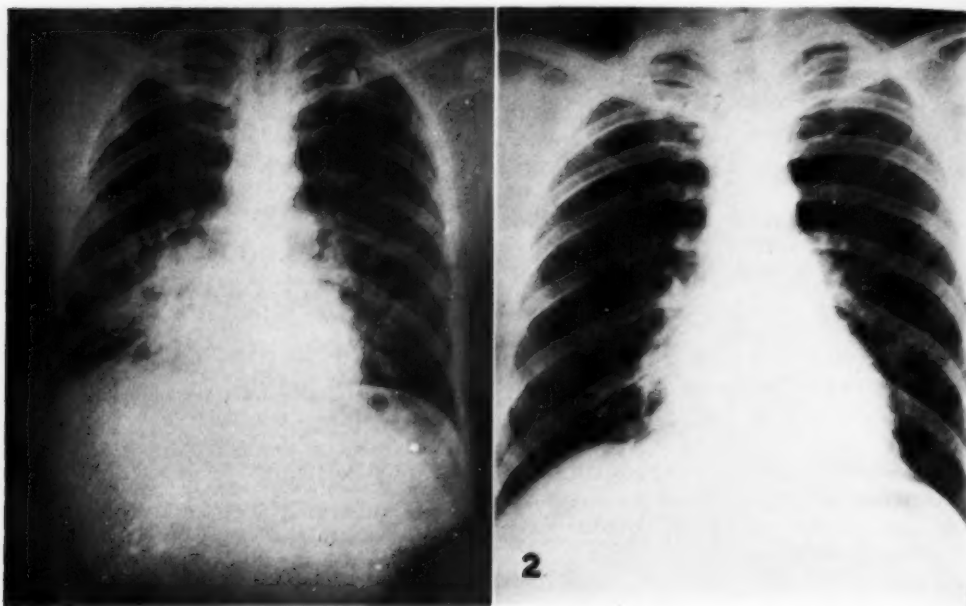


Fig. 1. Lung changes thirty-six hours after immersion.

Fig. 2. The same lung fields three weeks later.

about the same salt content as sea water (3.6 per cent salt).

Our patient was submerged in the Athletic Club Pool, which, as shown by the above report, had about the same salt content as sea water, with sodium chloride, 7 gm. per 250 c.c. of water and other salts in much smaller amounts. We are inclined to believe that the salt content of the water could play but little part, if any, in producing the abnormal changes in the patient's lungs. The water did not contain chloramine, which could act as an irritant factor. Nor do we believe that the salt water of the pool or water alone could produce lung shadows of the density observed on our roentgenograms.

Two water phantoms were examined, one containing water from the New Orleans Athletic Club Pool, the other containing tap water. The shadows cast by both were alike. Of the different salts contained in sea water, sodium chloride predominates, amounting to 7 gm. per 250 c.c. of water. The approximate absorption rate of sodium chloride, taking beryllium as a standard of

one (9), is as follows: sodium 10.463; chlorine 61.651. Since there is but one molecule of sodium and one molecule of chlorine, the total absorbability rate of these two molecules is 72.114, insufficient to cast any appreciable shadow within the bronchial system. In comparing sodium bromide, having an absorbability rate of 1051.792, to sodium chloride, which has the rate of 72.114, we find that sodium bromide should cast a shadow fourteen times greater.

Nor are we inclined to believe that bronchopneumonia was the cause of the lung changes, since Trocmé and Lafarie showed that in their three cases the pulmonary changes were greatest immediately following drowning and rapidly subsided in subsequent radiographic examinations.

Atelectasis as a sole cause of abnormal lung shadows was also considered. We feel, however, that this is probably at most an associated factor, since necropsies on both men and animals have demonstrated the rapid development of pulmonary edema.

It would seem to us from the available evidence that the abnormal radiographic shadows seen in the lungs of our patient during recovery from drowning were probably due to pulmonary edema. This conclusion is based on our personal observation and also on the postmortem findings of pulmonary edema in the lungs of drowned human beings and animals reported by different authors. We are unable, however, to exclude small areas of associated segmental atelectasis as a contributing factor.

#### SUMMARY

A brief report has been made of the roentgenographic and clinical findings in a patient who recovered after submersion in water for an unknown period of time.

An attempt has been made to explain the abnormal radiographic images in the lungs. They are believed to be due primarily to pulmonary edema.

#### SUMARIO

#### Alteraciones Radiográficas en los Pulmones Durante la Reposición de la Asfixia por Sumersión

En un enfermo que se repuso después de haber estado sumergido en el agua durante un período desconocido de tiempo, las radiografías torácicas tomadas a las treinta y seis horas del rescate revelaron opacidades moteadas de los pulmones con zonas de confluencia en los dos tercios interiores de los campos pulmonares, en ambas regiones pericardíacas. Sucesivos estudios roentgenológicos mostraron desaparición cada vez mayor de dichos hallazgos hasta

que, al cabo de tres semanas, ya no cabía distinguir anomalías dotadas de mayor importancia.

A base de sus propias observaciones, comprendiendo el análisis químico del agua de la piscina en que sobrevino el accidente, y de los hallazgos autopsícos experimentales comunicados por otros, opinan los AA. que las anómalas imágenes radiográficas en los pulmones proceden primordialmente del edema pulmonar.

#### REFERENCES

1. TROCMÉ, P., AND LAFARIE, G.: Sur certains aspects radiologiques des poumons de noyés après réanimation. *Rev. de la tuberc.* 11: 87-93, 1947.
2. SANTE, L. R.: Principles of Roentgenological Interpretation. Ann Arbor, Mich., Edwards Brothers, Inc., 1947 ed., p. 196.
3. SANTE, L. R.: Personal communication, Dec. 21, 1949.
4. KARPOVICH, P. V.: Water in the Lungs of Drowned Animals. *Arch. Path.* 15: 828-833, 1933.
5. SWANN, H. G., BRUCER, M., MOORE, C., AND VEZIEN, B. L.: Fresh Water and Sea Water Drowning: A Study of the Terminal Cardiac and Biochemical Events. *Texas Rep. Biol. & Med.* 5: 423-437, 1947.
6. COT, C.: Les asphyxies accidentelles. Paris, N. Maloine, Ed., 1931.
7. JETTER, W. W., AND MORITZ, A. R.: Changes in the Magnesium and Chloride Contents of Blood from Drowning in Fresh and in Sea Water. *Arch. Path.* 35: 601-610, 1943.
8. LOUGHEED, D. W., JAMES, J. M., AND HALL, G. E.: Physiological Studies in Experimental Asphyxia and Drowning. *Canad. M. A. J.* 40: 423-428, 1939.
9. MENVILLE, LEON J.: Experimental Work Bearing upon the Standardization of the Absorptive Powers of the X-rays by Salts of the Various Metals. *Radiology* 3: 118-127, 1924.

Charity Hospital of Louisiana  
New Orleans 12, La.

# Tuberous Sclerosis, A Neurocutaneous Syndrome

## Report of a Case<sup>1</sup>

LT. COMDR. G. CHARLES BUDENZ (MC), U.S.N.<sup>2</sup>

**T**UBEROUS SCLEROSIS is a rare disease of protean manifestations, involving primarily the skin and nervous system. It is one of the congenital ectodermoses (neurocutaneous syndromes), among which are von Recklinghausen's neurofibromatosis, angiomas cerebri, and von Hippel-Lindau's disease. As this group has a com-

mon origin, and the family history was not significant. He had not entered school until he was eight years old, because up to that age only his mother could understand his speech. He left school at the age of seventeen without completing the eighth grade. For many years he had suffered from sinusitis and had undergone various operations on the nasal septum and sinuses. Between 1929 and 1932 he had experienced repeated febrile episodes of un-

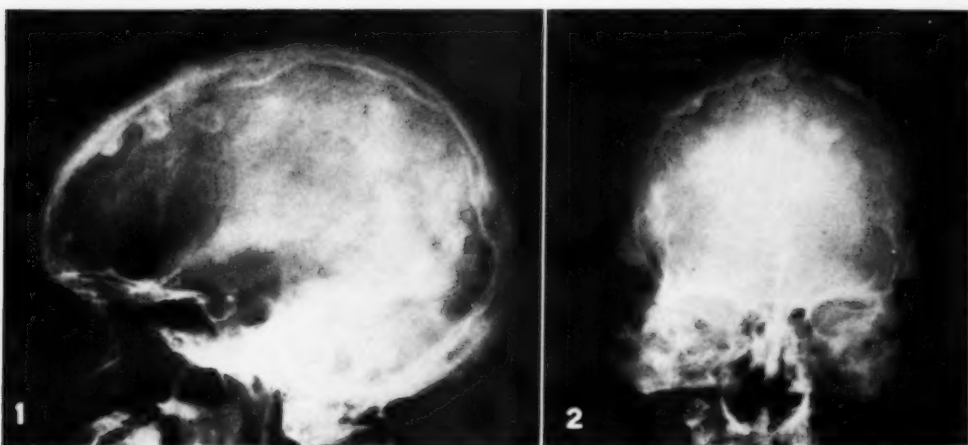


Fig. 1. The calvarium is of increased thickness, with irregular outer table and exostoses of the inner table especially of the frontal bone. There are scattered areas in which the bone is unusually dense.

Fig. 2. The exostoses of the inner table lie to the right and left of the mid-line.

mon origin in the ectoblast, it is not unusual to find some overlapping of these entities. The following case is reported to show the occurrence of skin and osseous lesions such as are found in neurofibromatosis in a case of tuberous sclerosis.

### CASE REPORT

O. L. L., a 38-year-old white veteran, entered the hospital in February 1949 for repair of a left inguinal hernia. Due to a history of chronic sinusitis, an x-ray study of the sinuses was undertaken. The unusual appearance of the cranial vault on these films led to further studies.

The patient had only meager recollections of his

known origin, lasting two or three days, with temperatures ranging up to 104°.

During the war the patient had served in Africa, Corsica, and Italy. While in Italy he had been hospitalized for one month because of recurrent dizzy spells, which responded to rest. In 1947 he had a sudden profuse hemorrhage per rectum. Roentgen studies at another hospital had shown multiple polyps, and a total colectomy was done. Several polyps were found to have undergone malignant change.

The patient was married and had a two-year-old child, apparently normal.

On physical examination the height and weight were found to be normal. The head did not appear unusual on cursory examination, but palpation showed the calvarium to be very irregular, with

<sup>1</sup> Accepted for publication in December 1949. The opinions expressed in this article are those of the author and do not necessarily represent those of the Navy Department.

<sup>2</sup> Now the Albert Sotland Fellow in Therapeutic Radiology, Los Angeles Tumor Institute, Los Angeles, Calif.



Fig. 3. There is a circular tumor 3.5 cm. in diameter in profile with the left sternoclavicular joint. A soft-tissue shadow is present in the right supraclavicular area. The inferior borders of some of the ribs are irregularly thickened.

numerous small bony nodules over the frontal, parietal, and occipital regions. These nodules were not movable, forming a part of the outer table of the skull. There was a confluent induration of the skin on both sides of the nose, extending infraorbitally, but no nodules were palpable in this region. On the face were several pigmented nevi and fleshy papillomas.

A number of small, non-tender cutaneous nodules were present, mainly in the hip regions, but also scattered over the abdomen, thighs, and legs. One nodule over the right tibia was tender. On questioning, the patient stated that occasionally a nodule became inflamed, with discharge of pus. Scattered papillomas occurred over the back. There were small areas of decreased pigmentation on the posterior surfaces of the arms and forearms.

The deep and superficial reflexes and sensory tests were normal. An audiogram showed slight decrease of hearing in the higher pitches.

The chest and cardiovascular findings were normal. Abdominal findings were those incident to the earlier colectomy.

The Kahn test was negative on two occasions. The red cell count was 4,500,000. White cells numbered 12,900, with 62 per cent segmented forms, 3 per cent band forms, 30 per cent lymphocytes, 1 per cent eosinophils, and 4 per cent monocytes. The blood chemistry was within normal limits.

Biopsies of two pigmented lesions on the face showed them to be benign pigmented nevi. A nodule from the abdominal wall proved to be a chronically inflamed sebaceous gland. The tender nodule on the leg was a xanthoma. A nodule from the right hip was a fibroma.

Roentgen examination (Figs. 1 and 2) showed the calvarium to be of increased thickness, with widening of the diploe. The inner and outer tables were irregular in outline, and several exostoses of the



Fig. 4. Right humerus and femur. The diaphyses show thickening of the cortex and coarseness of the bone trabeculae.

inner table were present in the frontal region, both to the right and left of the mid-line. The largest of these extended 1.5 cm. inward from the inner table. In scattered areas, particularly in the occipital region, the bone was unusually dense. No calcifications could be demonstrated in the substance of the brain. The sella turcica was of normal size, and the facial bones were of normal appearance.

Chest examination (Fig. 3) showed a normal heart and aorta. A circular tumor, 3.5 cm. in diameter, was seen in profile with the left sternoclavicular joint, adjacent to the anterolateral surface of D-5, without erosion of the vertebral body. In the right supraclavicular region was a soft-tissue shadow located between the lung tissue and the chest wall. The lungs were otherwise clear. There was erosion or "notching" of the inferior margins of several ribs, similar to that seen in coarctation of the aorta. Other ribs showed a wavy, irregular thickening of the lower margins. This cortical thickening involved areas from 2 to 10 cm. in length.

The spine and pelvis were normal. The diaphyses of the humeri and femora (Fig. 4) showed thickening and irregularity of the cortex, with coarseness of the bone trabeculae. The cancellous extremities of the bones were not involved. The forearms, hands, legs, and feet were normal.

The gastro-intestinal tract was normal except for the ileostomy and absence of the colon. The urinary tract likewise was normal, though the bladder showed surgical distortion.

#### DISCUSSION

The syndrome of tuberous sclerosis was originally described by Bourneville in 1880. The disease is rare in North America, but is more prevalent among the poorer classes of Europe and Australia. It is generally considered a dysplasia of ectodermal elements, though tumors may be found within regions derived from the mesoderm. The disease has been termed neoplastic, and true neoplasms do occur. The anatomical changes probably date back to early intra-uterine life, but do not terminate with birth. Though it does not seem likely that new foci develop after birth, preformed foci are capable of further growth, and may not become manifest until puberty or even adult life, cases having been reported in the sixth and seventh decades. Though the disease has definite hereditary tendencies, it may occur sporadically.

The three outstanding manifestations of tuberous sclerosis are: epilepsy, mental retardation, and adenoma sebaceum. Other features frequently reported are congenital tumors of the retina, termed phacomias by vanHoeve, subungual fibromas, and various congenital stigmata such as high-arched palate, cleft palate, simian hands, multiple skin nodules similar to neurofibromatosis. Visceral tumors such as rhabdomyoma, hypernephroma, renal liposarcoma, and multiple polyposis of the colon are occasionally found. Cystic disease of the lung, characterized by an irregular honeycomb-like pattern, is a rare finding. Bone lesions are frequent in the skull, but unusual elsewhere. Cases of a mild nature occur, in which only one of the cardinal features may be found.

Epilepsy is often the first symptom, and may be of the grand mal, petit mal, or jacksonian type. Attacks may be very frequent, even constituting a *status epilepticus*, or there may be long remissions.

There is almost always some delay in talking and walking but slight retardation may go unrecognized. Psychically the patient may appear normal in infancy with subsequent deterioration, but mental deficiency from birth is usual.

Pathologically, tuberous sclerosis is characterized by the presence of irregular tumors, 0.5 to 3.0 cm. in diameter, in the cerebral hemispheres and in the walls of the third and lateral ventricles. The pyramidal cells and glial elements are involved. The pyramidal cells are disoriented, atrophied, and reduced in number, and the neuroglia exhibits marked overgrowth. Giant cells are a constant finding in and about the tumors, but their origin is not known. The nodules may calcify or undergo cystic degeneration, though Dickerson failed to find calcified nodules in 5 cases seen at autopsy, in 3 of which there were typical skull changes. The irregular appearance of the nodules on the floor of the ventricles gives the surface an appearance which has been compared to "candle gutterings." The nodular areas in the region of the hypothalamus apparently are responsible for the bouts of fever that may occur in these patients.

Adenoma sebaceum, or the *nevus multiplex* of Pringle, consists of a symmetrical butterfly distribution of small nodular tumors over the nose, cheeks, and chin. These usually do not appear until the fourth or fifth year of life. The color varies from that of normal skin to a deep red, depending on the vascularity of the tumors. The nodules consist of hypertrophic sebaceous glands and newly formed connective tissue; the latter may compress and almost completely replace the glandular elements. Other skin lesions, such as nodules, *café au lait* spots, vitiligo, and *peau de chagrin*, a rough irregular zone of thickened skin usually on the back, are also found. The skin lesions may be identical with those of neurofibromatosis.

The skeletal changes have been described by numerous observers. Gottlieb

and Lavine found periosteal thickening of the metacarpal and metatarsal bones and their associated phalanges. The cortical layers showed a generalized fragmentation. The cranial bones showed peculiar mottling, with indistinct islands of increased density alternating with rarefied areas. Both internal and external tables were thickened, and exostoses of the inner table were present.

Dickerson reported the presence of patchy zones of increased density in the calvarium in half his cases, consisting of "areas of osteosclerosis, in which the marrow spaces of the cancellous bone in the diploic area had largely disappeared, owing to a concentric displacement of bone on the previous trabeculae. There was no evidence of neoplasm. It was evident that in the region of osteosclerosis the marrow was fatty instead of cellular." Rarefied areas about the zones of increased density were not observed.

Ackermann reported a case demonstrating, in addition to cystic changes in the lungs, a fairly large erosion of the first lumbar vertebra, large rarefied areas within both iliac bones, with smaller cyst-like areas in the left ilium, and multiple cysts in the femoral necks and juxtatrochanteric portions of the shafts. Surrounding these cystic areas was a narrow zone of sclerotic bone. The diaphyses of both femora showed a diffuse fibrillation of the cortex with thickening of the bone trabeculae.

The case herein presented represents a *forme fruste* type of disease. Epilepsy so far has not occurred. Mental retardation is represented by the delay in talking and difficulty in school. The butterfly induration of the skin of the nose and infraorbital regions is suggestive, though not typical, of adenoma sebaceum. Fevers of unknown origin occur in this disease, and also multiple polyposis of the colon. The skin nodules, the thickening and notching of the ribs, the mediastinal tumor, and the cortical changes of the humeri and femora are suggestive of the generalized neurofibromatosis of von Recklinghausen,

though, as stated before, the neurocutaneous syndromes are not sharply demarcated.

#### SUMMARY

A case of tuberous sclerosis is presented with osseous lesions in the calvarium, ribs, humeri and femora. Various skin lesions, a mediastinal tumor, and multiple polyposis of the colon were also present. The osseous and skin manifestations indicate the close relationship between tuberous sclerosis and neurofibromatosis.

1407 S. Hope St.  
Los Angeles 15, Calif.

#### BIBLIOGRAPHY

- ACKERMANN, A. J.: Pulmonary and Osseous Manifestations of Tuberous Sclerosis. *Am. J. Roentgenol.* **51**: 315-325, March 1944.
- AEGERTER, E. E., and SMITH, L. W.: Case of Diffuse Neurofibromatosis Involving the Cranial, Peripheral, and Sympathetic Nerves, Accompanied by Tumor of the Hypothalamus. *Am. J. Cancer* **31**: 212-220, October 1937.
- BERKOWITZ, N. J., and RIGLER, L. G.: Tuberous Sclerosis Diagnosed with Cerebral Pneumography. *Arch. Neurol. & Psychiat.* **34**: 833-838, October 1935.
- CAMP, J. D.: Pathologic Non-Neoplastic Intracranial Calcification. *J. A. M. A.* **137**: 1023-1031, July 17, 1948.
- DICKERSON, W. W.: Characteristic Roentgen Changes Associated with Tuberous Sclerosis. *Arch. Neurol. & Psychiat.* **53**: 199-204, March 1945.
- DRAKE, R. L.: Case of Tuberous Sclerosis with Unusual Clinical Findings. *Arch. Neurol. & Psychiat.* **34**: 681-682, September 1935.
- ENGLISH, D. A.: Tuberous Sclerosis. Report of a Case. *Arch. Pediat.* **66**: 24-29, January 1949.
- GOTTLIEB, J. S., and LAVINE, G. R.: Tuberous Sclerosis with Unusual Lesions of the Bones. *Arch. Neurol. & Psychiat.* **33**: 379-388, February 1935.
- HEUBLEIN, G. W., PENDERGRASS, E. P., and WIDMANN, B. P.: Roentgenographic Findings in the Neurocutaneous Syndromes. *Radiology* **35**: 707-727, December 1940.
- HOLT, J. F., and WRIGHT, E. M.: Radiologic Features of Neurofibromatosis. *Radiology* **51**: 647-663, November 1948.
- MILLER, A.: Neurofibromatosis with Reference to Skeletal Changes, Compression Myelitis, and Malignant Degeneration. *Arch. Surg.* **32**: 109-122, January 1936.
- SACHS, M. D., and SHASKAN, D. A.: Tuberous Sclerosis. *Am. J. Roentgenol.* **52**: 35-39, July 1939.
- SCHWARZ, H., and ABRAMSON, H.: Neurocutaneous Syndromes in Childhood. *J. Pediat.* **3**: 586-607, October 1933.
- SKER, J.: Adenoma Sebaceum (Pringle), von Recklinghausen's Disease, Subungual Fibromatosis Associated with Epilepsy or Tuberous Sclerosis—A Symptom Complex. *Urol. & Cutan. Rev.* **42**: 110-114, February 1938.
- STEWART, H. L., and BAUER, E. L.: Tuberous Sclerosis. *Arch. Path.* **14**: 799-809, December 1932.
- WALSH, M. N., KOCH, F. L. P., and BRUNSTING,

H. A.: Syndrome of Tuberous Sclerosis, Retinal Tumors, and Adenoma Sebaceum. Report of a Case. Proc. Staff Meet., Mayo Clinic 13: 155-160, March 9, 1938.

YAKOVLEV, P. I., AND GUTHRIE, R. H.: Congenital Ectodermoses (Neurocutaneous Syndromes) in Epileptic Patients. Arch. Neurol. & Psychiat. 26: 1145-1194, December 1931.

#### SUMARIO

##### Esclerosis Tuberosa, Síndrome Espontáneo. Historia Clínica

Preséntase un caso de esclerosis tuberosa con lesiones óseas del calvario, costillas, húmeros y fémures. En el enfermo había además varias lesiones cutáneas, un tumor del mediastino y poliposis múltiple del colon. Las manifestaciones óseas y cutáneas indican la íntima relación entre la esclerosis tuberosa y la neurofibromatosis.



# Traumatic and Related Types of Diaphragmatic Hernia<sup>1</sup>

FRANK ISAAC, M.D., FRANKLIN B. WILKINS, M.D., and JOSEPH WEINBERG, M.D.

Van Nuys, Calif.

WITH THE INCREASINGLY frequent use of roentgen rays in medical and surgical diagnosis, the incidence of diaphragmatic hernias is now known to be considerably higher than was believed two or three decades ago. This increase in incidence is due undoubtedly to the relatively high frequency with which esophageal hiatal hernias are found in routine gastro-intestinal examinations. These account for the overwhelming majority of all diaphragmatic hernias. Leaving the congenitally short esophagus and thoracic stomach out of consideration, for these are not really hernias, hiatal hernia is always acquired. It is most often found in the middle-aged male, especially in the obese, and usually involves only a relatively small portion of the fundus of the stomach.

The non-hiatal hernias, on the other hand, often involve a large portion of the abdominal viscera. Of these, some are congenital and occur through developmentally weak spots of the diaphragm, the foramen of Bochdalek or of Morgagni, or as a result of congenital absence of a portion of the leaf. Of more common occurrence is the acquired hernia which can be definitely traced to actual trauma.

In spite of the fairly large volume of literature on this general subject, comparatively little attention has been paid until recently to post-traumatic hernia. Jenkinson (1), reviewing some 25 cases of hernia in 1925, "failed to find any instance where trauma played an important part in the etiology." He believed that congenital weakness was present in every case and trauma was simply the precipitating factor. On the other hand, Harrington and Kirklin in 1938 (2), and Harrington in

1940 and again in 1943 (3, 4) emphasized the great clinical and surgical importance of trauma as an etiologic factor. It is probable that while many of the congenital hernias are present only as potential hernias and are actually brought about by trauma, a large number of the non-hiatal diaphragmatic hernias are directly attributable to the effect of injury, specifically laceration of the diaphragm.

The non-hiatal diaphragmatic hernias are practically always found on the left. Their infrequent occurrence on the right, as has often been pointed out, is probably due to the protection afforded by the liver. The congenital variety is often enclosed in a sac of pleura and peritoneum. The purely traumatic type has no sac and the abdominal viscera are in direct contact with the lungs. Both varieties often involve a large portion of the gastro-intestinal tract, quite frequently the spleen, and at times the pancreas and even the left kidney. Occasionally, however, the hernia will contain no viscus and will consist simply of a mass of omentum. These hernias are often misdiagnosed or completely missed for months or even years. They may masquerade as mere diaphragmatic deformities, unexplained pulmonary densities, or even pulmonary tumors. The diagnosis is usually missed simply because hernia is not considered as a possibility.

## CLINICAL AND ROENTGENOLOGIC FEATURES

The hernia may be asymptomatic and the patient may present himself with entirely unrelated complaints or the symptoms may be vague, bizarre, and not characteristic of any particular disease entity. Often the symptoms suggest cardiac or

<sup>1</sup> From the Departments of Radiology and Surgery, Birmingham Veterans Administration Hospital, Van Nuys, Calif. Sponsored by the Veterans Administration and published with the approval of the Chief Medical Director. The statements and conclusions published by the authors are a result of their own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

Accepted for publication in February 1950.

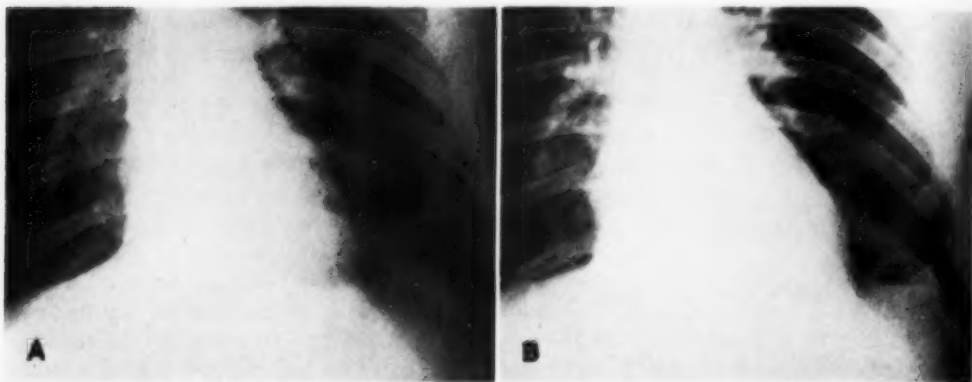


Fig. 1. Case I. A. Routine pre-employment film (Sept. 4, 1946) showing deformity of left dome of diaphragm with wedge-shaped area of density.

B. Admission film (June 10, 1947) showing same basal density, now containing an air-fluid level.

respiratory disease. Only in rare instances are they referable to the gastro-intestinal tract. On the other hand, the patient may be admitted to the hospital with frank symptoms of intestinal obstruction or, at least, those of an acute abdominal emergency.

Kirklin and Hodgson (5), in a comprehensive review of the entire subject, state that the chest roentgenogram should be the initial step in the investigation of this type of hernia, which, of course, implies that the condition is suspected clinically. In our experience, it is most often the routine chest film itself which first directs attention to this possibility. If gas-containing stomach or intestinal loops are present in the thoracic cavity, the diagnosis is fairly obvious even to the uninitiated. Often, however, the roentgenogram will show nothing more than a sharp tenting of the left dome of the diaphragm, or obliteration of the costophrenic sulcus, such as might be the residua of an old pleuritis. Or there may be an unexplained density in the left base having the appearance of pneumonitis, but with no evidence of resolution in serial films obtained over a period of time. Again, there may be a large, well circumscribed spherical shadow in the left base, just above and inseparable from the diaphragm, simulating a pulmonary neoplasm. In the majority of cases, however, a history of trauma to the chest can be

obtained, and the roentgenogram, especially if taken with heavier penetration or with the Bucky diaphragm, may reveal old fractures involving the lower ribs.

It is well to emphasize that whenever a deformity of the left hemidiaphragm is found on the chest film, or there is an unexplained density in the left base partially obscuring the diaphragm, especially if associated with fractures of the lower ribs, diaphragmatic hernia should be suspected. An opaque examination of the colon followed by barium-meal examination of the upper gastro-intestinal tract will be sufficient in most of these cases to establish the diagnosis. If, however, the hernia is made up entirely of omentum, the opaque examination will not add to the information obtained from the plain chest film. This latter type of hernia usually presents itself as a well marginated spherical mass inseparable from the diaphragm in any projection.

At times, hernia may be confused with eventration of the diaphragm. A stomach which is herniated, partly because of partial mechanical obstruction and partly because of disturbed physiology, becomes markedly dilated, and the upper wall of the fundus closely simulates an unusually high diaphragm. The differential diagnosis can be readily made in most of these cases by artificial pneumothorax or pneumoperitoneum (6, 9).

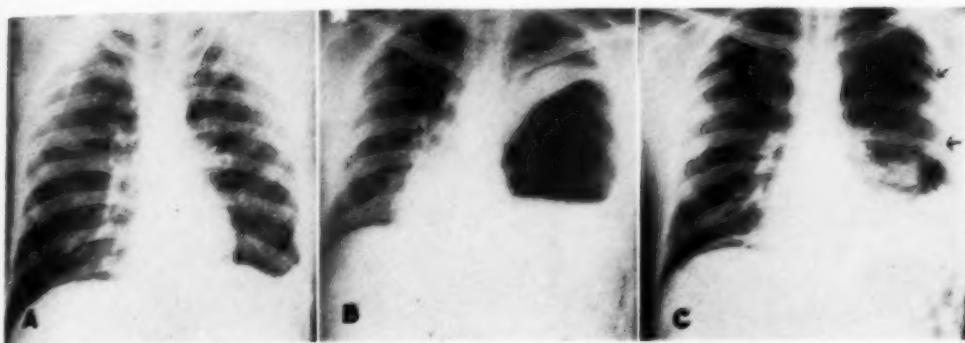


Fig. 2. Case II. A. Admission chest film (July 18, 1948). Left costophrenic angle obliterated, apparently by old adhesions.

B. Film obtained (Oct. 30, 1948) after a severe attack of vomiting following intravenous pyelography. Huge dilatation of stomach, with marked compression of left lower lobe and shift of mediastinum to the right.

C. Pneumoperitoneum induced after decompression of stomach. Note air under diaphragm on the right and in the thoracic cavity on the left.

#### CASE REPORTS

**CASE I (Fig. 1):** A 24-year-old male was admitted to the hospital complaining of severe cramp-like abdominal pain for thirty-six hours, and nausea and vomiting beginning several hours after the onset of pain. On examination he appeared acutely ill and there was tenderness over the entire abdomen, most marked in the right lower quadrant. There was moderate rigidity of the abdominal muscles; temperature and pulse were normal, but there was a leukocytosis of 17,500 with 83 per cent polymorphonuclears.

A chest roentgenogram revealed a triangular area of increased density in the left base, obscuring the dome of the diaphragm. In the upper part of this area was a large gas bubble with a fluid level. The possibility of an incarcerated loop of bowel above the diaphragm was suspected, but intra-abdominal obstruction was more strongly considered. The roentgenologic diagnosis was acute intestinal obstruction.

In view of the somewhat confusing clinical picture, a right lower quadrant incision was made to explore the appendix. When the appendix was found to be grossly normal, the left upper quadrant was explored. The splenic flexure was found to be passing through the diaphragm into the chest. Repair of the strangulated diaphragmatic hernia was done. Complete recovery followed.

**Comment:** This hernia is an example of one that had been masquerading as a diaphragmatic deformity for years following injury to the chest. Nine months prior to admission, this patient had a routine pre-employment chest film taken at this hospital. The increased density in the left base contained no gas shadow and was

interpreted at that time as deformity of the diaphragm due to old adhesions. Further questioning during the postoperative period brought out the fact that the patient had sustained a chest injury in an automobile accident several years previously. On closer examination, evidence of old rib fractures was found on Bucky films of the chest and abdomen.

**CASE II (Fig. 2):** A 30-year-old male was admitted to the Paraplegia Service for observation. Eight months previously, he was thrown from a motorcycle and sustained multiple skeletal fractures, including fracture of the spine resulting in loss of function of both lower extremities and loss of bladder and bowel control. There were also fractures of the 8th and 9th ribs on the left side.

A routine admission chest film showed the diaphragm to be in normal position, with only the left costophrenic angle obliterated, apparently by adhesions. In the course of study, excretory pyelography was done, which resulted in an attack of vomiting and excessive retching. Following this, the patient began to complain of increasing dyspnea. X-ray examination of the chest and abdomen revealed huge dilatation of the stomach, with a very large amount of gas and considerable fluid. The diaphragm appeared to be displaced upward to the level of the first interspace. The left lower lobe was densely compressed into a triangular band just below the clavicle. The mediastinum was markedly displaced to the right. The kidneys appeared in normal position and psoas outlines were normal. It was believed that this represented eventration of the diaphragm. However, to differentiate between eventration and actual herniation of the abdominal viscera through the diaphragm, the stomach was de-

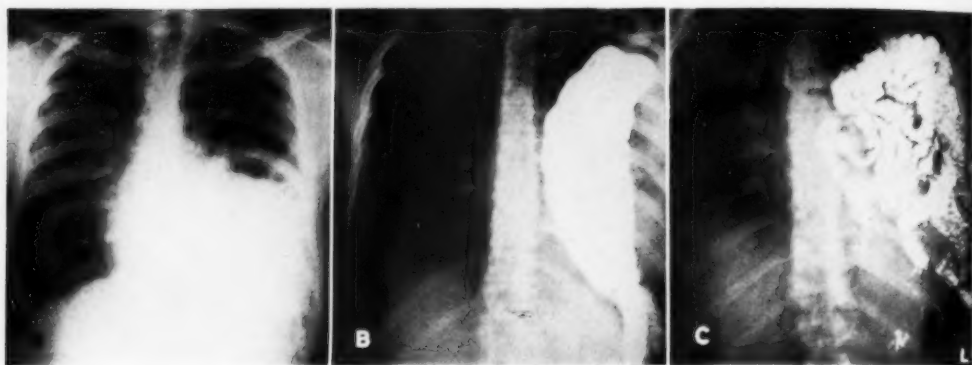


Fig. 3. Case III. A. Dense opacification of left lower lung field, obscuring diaphragm and left cardiac border, with curvilinear densities above, giving appearance of gas-filled intestinal loops.  
 B. Barium-enema study showing long loop of colon in the thoracic cavity.  
 C. Barium-meal examination showing a large portion of the small bowel in the thorax.

compressed by suction and pneumoperitoneum was induced. Air appeared under the right diaphragm, but on the left side the air was in the chest, indicating a definite rent in the diaphragm.

The diagnosis of diaphragmatic hernia was made and at operation, through an intercostal incision, the stomach, spleen, and a long loop of transverse colon with attached omentum were found in the left hemithorax. The diaphragm had a large stellate laceration, extending from the tendinous portion to the lateral and anterior chest wall. The patient had an uneventful convalescence.

*Comment:* In this case, the upper wall of the gastric fundus closely simulated an unusually high diaphragm. It was only because no possible explanation could be advanced to account for a sudden phrenic paralysis, and because the patient's symptoms were out of proportion to what one may expect in cases of eventration, that pneumoperitoneum was induced.

**CASE III (Fig. 3):** A 27-year-old male received a spine injury on Iwo Jima, March 4, 1945, a bullet fracturing the second lumbar vertebra, causing paraplegia below this level. Almost three years later, in the course of routine studies for poor bladder function, a large diaphragmatic hernia was discovered on the left. Although the hernia was producing no symptoms, the patient was admitted to the hospital for repair.

A roentgenogram of the chest on the day of admission revealed dense opacification of the lower half of the left lung, obscuring the diaphragm and the left cardiac border. Above this area were curvilinear densities with intervening radiolucencies, giving the appearance of gas-filled intestinal loops in the thoracic cavity. The mediastinal structures were

displaced moderately to the right. There was an old healed fracture of the 10th left rib in the posterior axillary line. A barium-enema study showed a long loop of the colon in the left hemithorax, with the splenic flexure just below the clavicle. Barium-meal examination showed the distal end of the esophagus to curve sharply upward and re-enter the thoracic cavity. The stomach, duodenal bulb, and the bulk of the small bowel were located in the thoracic cavity.

At operation through an intercostal incision, the stomach, most of the small intestine, the transverse colon, the omentum, and the spleen were found in the chest. The base of the left lung was atelectatic and densely adherent to the spleen and diaphragm. The diaphragmatic rent measured 20 cm. across and 10 cm. from before backward. Splenectomy had to be done; the gastro-intestinal tract was returned to the abdomen, and the diaphragmatic defect was closed.

*Comment:* The outstanding feature in this case was that most of the gastro-intestinal tract and the spleen must have been in the chest for a period of three years without giving rise to significant symptoms. This can probably be accounted for by the large size of the diaphragmatic rent and the consequent free movement of the viscera.

**CASE IV (Fig. 4):** A 51-year-old man entered the hospital for repair of bilateral recurrent inguinal hernias. He had also had intermittent asthmatic attacks for twenty-eight years, always quickly relieved by aminophyllin. Physical examination was not remarkable, except for bilateral inguinal hernias, which were easily reducible.

A routine admission chest film revealed an unusually high left diaphragm with the costophrenic angle obliterated. There were also considerable

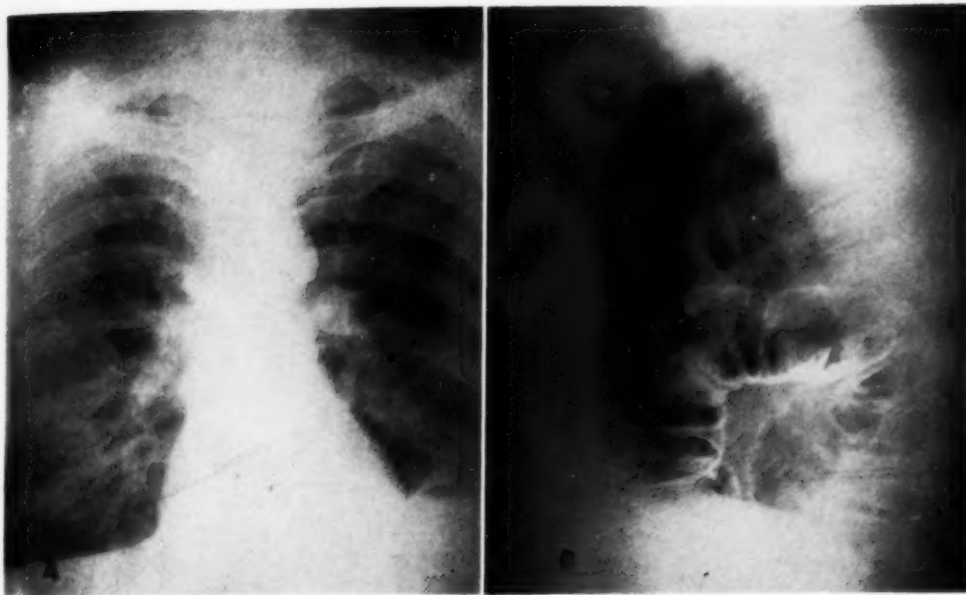


Fig. 4. Case IV. A. Admission film showing high left leaf of diaphragm and obliteration of costophrenic angle. There is considerable mottling in the left base, suggesting pneumonitis.  
B. Lateral view of chest after opaque enema and insufflation of air into the colon. There is a large loop of colon in the thorax.

streaking and mottling in the left base, just above the diaphragm, suggesting pneumonitis. Several rechecks at intervals of a few days disclosed very little change in the appearance of the chest, and the nature of the lesion in the left base was not clear either to the roentgenologist or to the clinician. Because of its relatively quiescent appearance, however, and the eagerness of the patient to return to work, a left hemiorrhaphy was done.

A postoperative chest film showed an increase in the mottling in the left base, and the appearance now suggested a possible lesion below the diaphragm. At this time, the investigation was carried further, and a barium enema was done. The splenic flexure was seen to extend high into the thoracic cavity. This had the appearance of a diaphragmatic hernia, although the exact location of the diaphragm could not be determined.

Surgical exploration through the 8th intercostal space revealed the presence of a loop of splenic flexure and a large congested spleen in the chest, these structures having entered through a 3-inch defect in the diaphragm at its attachment to the left chest wall. The hernia was reduced and the diaphragmatic defect repaired.

**Comment:** In this case there was no history of chest injury, and it is assumed that the opening represented a congenital defect due to persistence of the foramen of

Bochdalek. Failure to discover it earlier was due to the fact that it had not been considered as a diagnostic possibility in spite of the suggestive chest film.

**CASE V (Fig. 5):** A 59-year old man had been known to have an esophageal hiatal hernia for six years. He described his symptoms as epigastric distress after eating, worse when lying down. In his youth he had sustained a fracture of the clavicle and lower ribs on the left in a motorcycle accident. Sixteen months before admission, he was in a bus accident and was thrown forward, striking the seat in front of him with his head and chest.

A roentgenogram of the chest on admission revealed a large, round, well circumscribed mass in the left base laterally, about halfway between the anterior and posterior chest walls. It was believed that the mass represented herniation of the abdominal viscera through the diaphragm, although a solitary pulmonary metastasis or primary peripheral bronchogenic neoplasm could not be definitely ruled out.

Barium-enema and barium-meal examinations were negative except for a small esophageal hiatal hernia of the stomach. On fluoroscopy it was found that the mass was intimately connected with the diaphragm and was inseparable from it.

At operation, through the 7th intercostal space, a diaphragmatic hernia the size of a grapefruit was

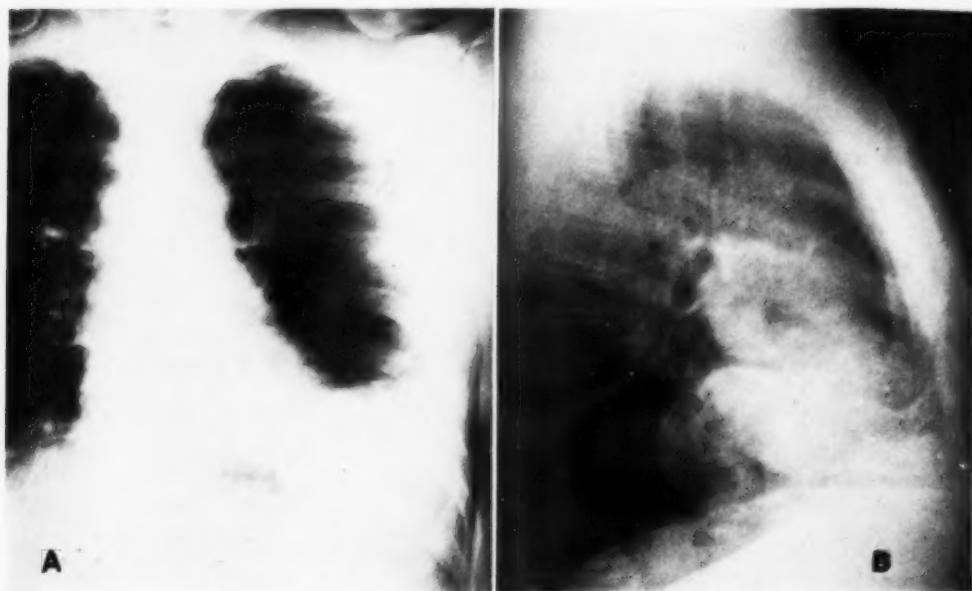


Fig. 5. Case V. Large spherical mass in left base immediately above and inseparable from the diaphragm.

found, with a sac consisting of pleura and peritoneum and filled with omentum. The actual muscular defect in the diaphragm extended from the tendinous portion of the leaf to the lateral chest wall. The hernia was reduced, redundant sac excised, and the diaphragm repaired. Convalescence was uneventful.

*Comment:* The presence of a definite sac consisting of pleura and peritoneum presumably speaks against the traumatic etiology and strongly suggests a congenital origin. Yet readings of chest films at a large university hospital one year previously did not report the presence of this hernia. It is possible that the hernia occurred through a congenital defect, the actual herniation taking place gradually over a period of many months following the more recent bus accident.

#### SUMMARY AND CONCLUSIONS

Diaphragmatic hernias are frequently encountered in modern roentgenologic practice. By far the most common variety is the esophageal hiatal hernia.

The non-hiatal hernias are frequently caused by direct trauma with actual laceration of the diaphragm, although some occur through pre-existing congenital weak spots

or as a result of absence of portions of the leaf. Diaphragmatic hernias are often asymptomatic and may go undiagnosed for considerable periods of time. The non-hiatal hernias frequently masquerade as other pulmonary or pleural lesions in the basal portion of the left lung field.

Pure omental hernias, as a rule, will present themselves as well margined, spherical masses just above the diaphragm.

Whenever a deformity of the left diaphragm is demonstrated in the chest film, or there is an unexplained density in the left base partially obscuring the diaphragm without other evidences of pulmonary infection, the possibility of diaphragmatic hernia should be considered.

Birmingham Veterans Administration Hospital  
Van Nuys, Calif.

#### REFERENCES

1. JENKINSON, E. L.: Lesions of the Diaphragm. *Am. J. Roentgenol.* 14: 16-19, July 1925.
2. HARRINGTON, S. W., AND KIRKLIN, B. R.: Clinical and Roentgenologic Manifestations and Surgical Treatment of Diaphragmatic Hernia, with a Review of 131 Cases. *Radiology* 30: 147-156, February 1938.
3. HARRINGTON, S. W.: Diagnosis and Treatment of Various Types of Diaphragmatic Hernia. *Am. J. Surg.* 50: 381-446, November 1940.

4. HARRINGTON, S. W.: Roentgenologic Considerations in the Diagnosis and Treatment of Diaphragmatic Hernia. *Am. J. Roentgenol.* **49**: 185-195, February 1943.
5. KIRKLIN, B. R., AND HODGSON, J. R.: Roentgenologic Characteristics of Diaphragmatic Hernia. *Am. J. Roentgenol.* **58**: 77-101, July 1947.
6. FAULKNER, W. B., JR.: Diaphragmatic Hernia and Eventration. Use of Pneumothorax in Differential Diagnosis. *Am. J. Roentgenol.* **45**: 72-73, January 1941.
7. CARMAN, R. D., AND FINEMAN, S.: Roentgenologic Diagnosis of Diaphragmatic Hernia, with a Report of Seventeen Cases. *Radiology* **3**: 26-45, July 1924.
8. CASE, J. T., AND UPSON, W. O.: Roentgenologic Aspects of Various Types of Hernia. *J. A. M. A.* **87**: 891-898, Sept. 18, 1926.
9. SANTE, L. R.: Pneumoperitoneum as an Aid in the Diagnosis of Sub-Diaphragmatic Conditions. *J. A. M. A.* **80**: 464-466, Feb. 17, 1923.
10. WEINBERG, J.: Diaphragmatic Hernia; Collective Review. *Internat. Abstr. Surg.* **72**: 445-452, 1941; in *Surg. Gynec. & Obst.*, May 1941.

## SUMARIO

## Formas Traumáticas y Otras Afines de Hernia Diafragmática

Las hernias diafragmáticas resultan frecuentes en la moderna práctica roentgenológica, siendo, con mucho, las más comunes las del hiato o abertura del esófago.

Las hernias no hiatales son frecuentemente ocasionadas por traumatismo directo con verdadera laceración del diafragma, aunque algunas ocurren a través de puntos vulnerables congénitos ya preexistentes o debido a ausencia de porciones de la hoja. Las hernias diafragmáticas son a menudo asintomáticas y pueden pasar sin diagnosticarse considerables períodos de tiempo. Las no hiatales son frecuentemente tomadas por otras lesiones pulmonares o pleu-

rales en la porción basal del campo pulmonar izquierdo.

Las hernias epiploicas puras se presentan, por regla general, en forma de tumefacciones esféricas bien marginadas precisamente más arriba del diafragma.

Siempre que se descubra una deformidad del lado izquierdo del diafragma en la radiografía torácica, o cuando hay una condensación inexplicada en la base izquierda que eclipsa parcialmente el diafragma sin otros signos de infección pulmonar, debe considerarse la posibilidad de hernia diafragmática.

Comunicanse cinco casos típicos.



# Skeletal Metastases in Carcinoma<sup>1</sup>

HERBERT L. ABRAMS, M.D.<sup>2</sup>

THE SKELETON is one of the two most important sites for the antemortem demonstration of cancer metastases. In cases of latent primary carcinoma manifested only by secondary deposits in the bones, the site of the primary lesion will be more readily ascertained if the diagnostic work-up is based on a sound appraisal of the incidence of skeletal metastases. The patient who is sent to the radiologist because of back pain, and who is discovered to have a destructive lesion in his vertebrae, presumably metastatic, presents to the clinician the problem of tracking down a hidden source. The latter will be directed in his search by his conception, or misconception, of the primary sites from which carcinomas commonly metastasize to bone. In particular, he is likely to exclude from consideration such sites as the stomach, colon, rectum, pancreas, uterus, bladder, and ovary, or at least to relegate them too far into the background of his thinking.

There is a voluminous literature on the incidence of metastases in carcinoma. In the present study, an attempt has been made to relate incidence of skeletal metastases found at autopsy to the estimated prevalence in the population of carcinoma arising from different primary sites.

## METHOD AND RESULTS

The metastases in 1,000 consecutive cases of malignant neoplasms of epithelial origin autopsied at the Montefiore Hospital<sup>3</sup> between 1943 and 1947 were analyzed (1). In every instance, gross and microscopic studies of bone for metastases were undertaken. Sections of thoracic and lumbar vertebral bodies were obtained routinely, and where clinical information warranted it, further studies were made.

TABLE I: SKELETAL METASTASES IN 1,000 CONSECUTIVE CASES OF CARCINOMA

Site of Origin	Number of Cases	Number with Metastases
Prostate	19	16 (84%)
Breast	167	122 (73%)
Thyroid	10	5 (50%)
Lung	160	52 (32.5%)
Bladder	19	5 (26%)
Kidney	34	8 (23.5%)
Uterus	23	5 (22%)
Pancreas	32	4 (15.5%)
Rectum	87	11 (12.5%)
Stomach	119	13 (11%)
Ovary	64	6 (9%)
Colon	118	11 (9%)
Esophagus	17	2
Tongue	7	2
Larynx	14	1
Cervix	13	1
Others	97	8
Total	1,000	272

The skeletal metastases were tabulated and the incidence for each primary site was determined. The results are presented in Table I. Primary sites are listed in descending order of frequency (percentage) of metastases. Of 1,000 carcinomas, 272 were found to have metastasized to bone. There were 10 primary sites with bone metastases in more than 10 per cent of the cases.

## FREQUENCY OF SKELETAL METASTASIS AT AUTOPSY: COMPARISON WITH THE LITERATURE

In Table II, the incidence of skeletal metastases at autopsy in cases collected from the literature has been summarized. In general, our figures were higher than those in other series. This was particularly true in carcinoma arising from the gastro-intestinal tract.

It has been assumed that gastro-intestinal carcinoma metastasizes to bone only in rare instances. Coley classifies gastric

<sup>1</sup> From the Medical Laboratory Divisions of the Montefiore Hospital, New York City. Accepted for publication in January 1950.

<sup>2</sup> Present address: Department of Radiology, Stanford University School of Medicine, San Francisco, Calif.

<sup>3</sup> It should be pointed out that the Montefiore Hospital is a hospital for the chronically ill, and that the material might be expected to differ in some respects from that in a hospital for the treatment of acute disease.

and colonic carcinoma as "ossophobe" (7), and Ewing does not even mention figures on the incidence of skeletal metastases from this source (14). Among 373 gastrointestinal carcinomas in our series, however, 41 (11 per cent) had metastasized to the skeleton. Although most figures are appreciably lower than ours in this respect, some reports have shown a comparable incidence of metastases (2, 4, 45).

TABLE II. SKELETAL METASTASES IN CARCINOMA: COLLECTED CASES FROM THE LITERATURE

Site of Origin	Number of Cases	Number with Metastases
Prostate (9, 19, 26, 30, 45)	382	192 (50%)
Breast (21, 26, 30, 45, 48)	828	291 (35%)
Kidney (10, 23, 26, 33, 39, 45)	341	113 (33%)
Lung (26, 32, 40)	2,829	581 (20.5%)
Thyroid (12, 13, 24, 25, 26, 31, 41, 43)	1,585	303 (19%)
Bladder (26, 28, 45)	176	21 (12%)
Pancreas (18, 26, 38, 45)	138	15 (11%)
Fundus uteri (26, 37, 45)	176	11 (6%)
Rectum (2, 4, 5, 46)	512	25 (5%)
Rectum and colon (2, 3, 4, 5, 26, 36, 45, 46)	1,850	67 (3.5%)
Ovary (16, 26, 45)	125	4 (3%)
Stomach (15, 16, 26, 38, 42, 45, 47)	1,359	35 (2.5%)

RELATIVE FREQUENCY OF SKELETAL METASTASES FROM DIFFERENT PRIMARY SITES IN THE GENERAL POPULATION

If one attempts to relate the incidence of skeletal metastases as found in our series to the estimated incidence in the population of carcinoma arising from different primary sites, some interesting findings emerge. In Table III, primary sites are listed in descending order of frequency of metastases in the population, as determined by multiplying figures on the incidence<sup>4</sup> of carcinoma per hundred thousand population (20, 34) by the percentage of skeletal metastases at autopsy, as noted in Table I. By taking into account incidence of carcinoma in the population, the relatively high percentage of metastases of thyroid carcinoma, for example, is more than balanced by the more frequent occur-

<sup>4</sup> The figures used were estimates of the incidence in the population of New York and Connecticut of carcinomas arising from different primary sites. An average was determined in drawing up Table III.

TABLE III: COMMON SOURCES OF SKELETAL METASTASES FROM CARCINOMA:

(Projected Listing in Order of Frequency)\*

Order of Frequency	General Population	Male Population	Female Population
1	Breast	Prostate	Breast
2	Prostate	Lung	Uterus
3	Lung	Bladder	Colon
4	Colon	Stomach	Stomach
5	Stomach	Rectum	Rectum
6	Bladder	Colon	Bladder
7	Uterus	Kidney	Thyroid
8	Rectum	Pancreas	Ovary
9	Thyroid	Thyroid	Lung
10	Kidney		Kidney
11	Ovary		

\* This list was compiled by multiplying figures on incidence of carcinoma per hundred thousand general population, male population, and female population, by the percentage of skeletal metastases found at autopsy as noted in Table I.

rence of carcinoma of the colon. Thus, if there are 9 per cent metastases to bone from 27 carcinomas of the colon per one hundred thousand of population, the absolute number of metastases will be about four times as great as the 50 per cent metastases from 1.3 thyroid carcinomas per one hundred thousand population.

In Table III, the common primary sites of skeletal metastases are also listed for the male population and the female population in order of frequency. In the female, the breast is, of course, the commonest primary site of metastasis to bone. The uterus, colon, and stomach follow in that order. The thyroid is seventh on the list, and the kidney is tenth. In the male, the bladder and the stomach follow the lung and the prostate; the kidney is seventh on the list and the thyroid is ninth. Among the male population, there will be twenty times as many skeletal metastases from carcinoma of the stomach as from carcinoma of the thyroid, and six times as many from carcinoma of the lung as from carcinoma of the kidney. In the female population, there will be almost as many skeletal metastases from ovarian carcinoma as from thyroid, and more from the ovary than the kidney.

These figures are, of course, hypothetical. The population incidence figures were derived from only two states, and there is significant geographic variation in the prevalence of carcinoma (8). Further-

more, the number of cases of carcinoma arising from certain primary sites was too small in our series to permit generalization, though for carcinoma of the breast, lung, stomach, colon, and rectum, the figures are probably significant. In such sites as the prostate, thyroid, bladder, kidney, and pancreas, however, there was some degree of correspondence to the figures in the literature reviewed; if we were to substitute the figures from Table II (average figures from the literature) in compiling the statistics on population incidence of metastases from these primary sites, the only effect on Table III would be to move the bladder from the sixth to the eighth place on the list for the general population, the kidney to the ninth, and the thyroid to the eleventh.

Whether or not there is any justification for applying autopsy figures on metastases to incidence figures of carcinoma in the population should also be questioned. It may be well that many of the metastases occurred late in the course of the disease and could not therefore have been detected clinically. Furthermore, autopsy material is automatically selected material though the influence of the selection factors is difficult to evaluate.

The tables on incidence in the population provide, then, at best a gross approximation of the relative frequency with which metastases from different primary sites will be seen in the population.

The radiologist may comment that these metastases, present at autopsy, may have been microscopic or, if gross, may not have been detectable by roentgenograms. Commonly in his experience he has seen bone metastases from breast, lung, prostate, or kidney carcinoma. But metastases from the gastro-intestinal tract have been considered sufficiently rare in the past to warrant case reports.

In 10 of our 11 cases of carcinoma of the colon in which bone metastases were present, they were seen on the gross pathologic examination. The sites involved included the lumbar spine, the thoracic spine, the skull, innominate bone, the

femur, and the ribs. Skeletal roentgenograms were obtained antemortem in 7 cases, in 4 of which there was roentgen evidence of bone metastases.

In 11 of 13 cases of carcinoma of the stomach with bone metastases, the skeletal involvement was also seen on gross pathologic examination. Sites involved included the lumbar spine, the thoracic spine, the ribs, and iliac bones. Skeletal roentgenograms were obtained in 5 cases, in one of which there was roentgen evidence of bone metastasis.

In 10 of 11 cases of carcinoma of the rectum with bone metastases, the metastases were seen on gross pathologic examination. Sites involved included the lumbar spine, the thoracic spine, the ribs, the tibia, the fibula, the scapula, the skull, and the ilium. Skeletal roentgenograms were obtained in 9 cases and in 8 revealed evidence of metastases.

In 3 of 4 cases of carcinoma of the pancreas with bone metastases, the metastases were seen on gross pathologic examination. Sites involved included the lumbar and thoracic spine and iliac bone. Skeletal roentgenograms were obtained in 3 cases, with evidence of metastasis in one.

Thus, in 14 (58 per cent) of our 24 cases of carcinoma of the gastro-intestinal tract with bone metastases in which skeletal roentgenograms were obtained, the metastases were roentgenologically demonstrable.

#### SKELETAL METASTASES OF UNDETERMINED PRIMARY SITE

Certain probabilities are presented to the radiologist when he sees a lesion which he thinks is metastatic and the primary site of which is undetermined. An osteoblastic lesion in the male is statistically most likely to be prostatic in origin, but stomach, pancreas, and bladder should also be considered.<sup>5</sup> With an osteolytic lesion in the male, the lung is by far the most probable primary site. The bladder, gas-

<sup>5</sup> A discussion of the skeletal metastases of tumors of non-epithelial origin is not within the scope of this paper. Obviously, such tumors must be considered when evidence of skeletal involvement is present.

tro-intestinal tract, kidney, and thyroid must, however, be considered.

In the female, the breast is the most common primary source of bone metastases, whether osteolytic or osteoblastic. The uterus, gastro-intestinal tract, bladder, thyroid, and ovary follow in that order as possible sources, usually of osteolytic metastases. In the female, as compared to the male, the lung is negligible as a source of bone metastases and the pancreas even more so.

The fact that in one series of latent primary carcinoma, lung, stomach, pancreas, and prostate accounted for over two-thirds of the cases is a further point for consideration in weighing the most likely primary site of a metastatic lesion (17). Obviously, the location of the metastatic lesion will be an additional factor, though by no means a reliable one.

In 1940, Hubeny and Mass presented an analysis of the incidence of skeletal and pulmonary metastases which revealed "a considerable increase over previous estimates." The increased incidence of bone metastases they attributed to more thorough roentgen study and careful postmortem examination (26). Rigler, in the ensuing discussion, pointed out that autopsy figures were too low because the skeleton was not thoroughly studied in the routine examination. In the light of this, it is of interest that our figures are higher than those of Hubeny and Mass for every primary site, and in some instances represent "a considerable increase" over their figures. Factors which may account for the differences between our figures and those of other investigators have been discussed elsewhere (1). Suffice it to say that the reasons given by Hubeny and Mass for the apparent increased incidence of skeletal metastases seem applicable today. Our own figures, though generally higher than others, may still be only minimum; the actual incidence of skeletal metastasis is probably considerably higher, and will be determined with certainty only when a large series of cases is exhaustively investigated for bone metastases.

#### SUMMARY

1. In a series of 1,000 consecutively autopsied cases of carcinoma, there were 272 cases (27.2 per cent) with skeletal metastases.

2. Skeletal metastases occurred in over 10 per cent of carcinomas arising from ten different primary sites.

3. In general, these figures for skeletal metastases are higher than those in other series.

4. Such primary sites as the bladder, the uterus, the gastro-intestinal tract, and the ovary are more likely to account for skeletal metastases than has hitherto been thought.

Department of Radiology  
Stanford University School of Medicine  
San Francisco 15, Calif.

#### REFERENCES

1. ABRAMS, H. L., SPIRO, R., AND GOLDSTEIN, N.: Metastases in Carcinoma: Analysis of 1000 Autopsied Cases. *Cancer* 3: 74-85, 1950.
2. AUFSES, A. H.: Skeletal Metastases from Carcinoma of the Rectum. Report of Eight Cases. *Arch. Surg.* 21: 916-923, 1930.
3. BACON, H. E.: Unusual Sites of Metastasis from Carcinoma of the Rectum and Sigmoid Colon. *Pennsylvania M. J.* 43: 1573-1578, 1940.
4. BROWN, C. E., AND WARREN, S.: Visceral Metastasis from Rectal Carcinoma. *Surg., Gynec. & Obst.* 66: 611-621, 1938.
5. BUIRGE, R. E.: Carcinoma of the Large Intestine. Review of 416 Autopsy Records. *Arch. Surg.* 42: 801-818, 1941.
6. BUMPUS, H. C., JR.: Carcinoma of the Prostate. A Clinical Study. *Surg., Gynec. & Obst.* 32: 31-43, 1921.
7. COLEY, B. L.: Neoplasms of Bone and Related Conditions. New York, Paul B. Hoeber, Inc., 1949.
8. COLLINS, S. W., GOVER, M., AND DORN, H. F.: Trend and Geographic Variation in Cancer Mortality and Prevalence, with Special Reference to Gastric Cancer. *J. Nat. Cancer Inst.* 1: 425-450, 1941.
9. CONE, R. C.: Carcinoma of Prostate. Case Reports. *Urol. & Cutan. Rev.* 39: 101-104, 1935.
10. CREEVY, C. D.: Confusing Clinical Manifestations of Malignant Renal Neoplasm. *Arch. Int. Med.* 55: 895-916, 1935.
11. CROTTI, A.: Diseases of the Thyroid, Parathyroids, and Thymus. Philadelphia, Lea & Febiger 3d ed., 1938.
12. DINSMORE, R. S., AND HICKEN, N. F.: Metastases from Malignant Tumors of the Thyroid. *Am. J. Surg.* 24: 202-224, 1934.
13. EHRHARDT: Cited by Dinsmore and Hicken (12).
14. EWING, J.: Neoplastic Diseases. Philadelphia, W. B. Saunders Co., 4th ed., 1940.
15. FUENDELING AND HUNNICUTT: Cited by Liljencrantz (35).
16. GESCHICKTER, C. F., AND COPELAND, M. M.: Tumors of Bone. New York, Am. J. Cancer, 1936.

17. GEWANTER, A. P., MITCHELL, N., AND ANGRIST, A.: Latent Primary Carcinoma. *Arch. Path.* **35**: 66-84, 1943.
18. GRAUER, F. W.: Pancreatic Carcinoma. Review of 34 Autopsies. *Arch. Int. Med.* **63**: 884-898, 1939.
19. GRAVES, R. C., AND MILITZER, R. E.: Carcinoma of the Prostate with Metastases. *J. Urol.* **33**: 235-251, 1935.
20. GRISWOLD, M. H.: Evaluation of Cancer Control Methods in Connecticut. *J. A. M. A.* **138**: 881-884, 1948.
21. GROSS: Cited by Ewing (14).
22. HAAGENSEN, C. D.: Carcinoma of the Breast. *J. A. M. A.* **138**: 195-205, 1948.
23. HARVEY, N. A.: Kidney Tumors. A Clinical and Pathological Study with Special Reference to the "Hypernephroid" Tumor. *J. Urol.* **57**: 669-692, 1947.
24. HASSNER: Cited by Crotti (11).
25. HINTERSTOISSER: Cited by Dinsmore and Hicken (12).
26. HUBENY, M. J., AND MASS, M.: Roentgenologic Aspects of Metastases. *Radiology* **35**: 315-321, 1940.
27. JENKINSON, E. L.: Primary Carcinoma of the Gastro-intestinal Tract Accompanied by Bone Metastasis. *Am. J. Roentgenol.* **11**: 411-420, 1924.
28. JUDD, E. S., AND HAND, J. R.: Hypernephroma. *J. Urol.* **22**: 10-21, 1929.
29. KAUFMAN: Cited by Ewing (14).
30. KOCHER: Cited by Simpson (43).
31. JEWETT, H. J., AND STRONG, G. H.: Infiltrating Carcinoma of the Bladder: Relation of Depth of Penetration of the Bladder Wall to Incidence of Local Extension and Metastases. *J. Urol.* **55**: 366-372, 1946.
32. KOLETSKY, S.: Primary Carcinoma of the Lung: Clinical and Pathologic Study of 100 Cases. *Arch. Int. Med.* **62**: 636-651, 1938.
33. KOZOLL, D. D., AND KIRSHBAUM, J. D.: Relationship of Benign and Malignant Hypernephroid Tumors of Kidney. *J. Urol.* **44**: 435-449, 1940.
34. LEVIN: Cited by Haagensen (22).
35. LILJENCRANTZ, E., editor: *Cancer Handbook of the Tumor Clinic*, Stanford University School of Medicine. Stanford University Press, 1939.
36. MAYO, C. W., AND SCHLICKE, C. P.: Carcinoma of the Colon and Rectum. Study of Metastasis and Recurrences. *Surg., Gynec. & Obst.* **74**: 83-91, 1942.
37. MEIGS, J. V.: *Tumors of the Female Pelvic Organs*. New York, Macmillan Co., 1934.
38. MÜLLER: Cited by Coley (7).
39. NALLE, B. C.: Distant Metastases of 58 Renal Neoplasms: A Case Report of Secondary Metastatic Pulsations from a Renal Tumor. *J. Urol.* **57**: 662-668, 1947.
40. OCHSNER, A., AND DEBAKEY, M.: Carcinoma of the Lung. *Arch. Surg.* **42**: 209-258, 1941.
41. PEMBERTON, J. DE J.: Malignant Disease of the Thyroid Gland: A Clinical Consideration. *Ann. Surg.* **87**: 369-377, 1928.
42. SCHLESINGER: Cited by Jenkinson (27).
43. SIMPSON, W. M.: Clinical and Pathological Study of Fifty-Five Malignant Neoplasms of the Thyroid Gland. *Ann. Clin. Med.* **4**: 643-667, 1926.
44. THOMAS, G. L.: Metastasis to Bone in Gastro-intestinal Malignancy. *S. Clin. N. America* **26**: 692-694, 1946.
45. TURNER, J. W., AND JAFFE, H. L.: Metastatic Neoplasms: Clinical and Roentgenological Study of Involvement of Skeleton and Lungs. *Am. J. Roentgenol.* **43**: 479-492, 1940.
46. WARREN, S.: Studies on Tumor Metastasis. Distribution of Metastases in Carcinoma of the Large Intestine. *New England J. Med.* **209**: 167-173, 1933.
47. WARREN, S.: Studies on Tumor Metastasis. Metastases of Cancer of the Stomach. **209**: 825-827, 1933.
48. WARREN, S., AND WITHAM, E. M.: Studies on Tumor Metastasis. Distribution of Metastases in Cancer of the Breast. *Surg., Gynec. & Obst.* **57**: 81-85, 1933.

## SUMARIO

## Metástasis Esqueléticas en el Cáncer

El análisis de 1,000 casos consecutivos de neoplasias malignas observadas en la autopsia reveló 272, o sea 27.2 por ciento, con metástasis esqueléticas. Los tumores primarios de diez sitios, a saber, próstata, mama, tiroides, pulmón, vejiga urinaria, riñón, útero, páncreas, recto y estómago, tenían metástasis óseas en más de 10 por ciento de los casos. Otro tanto sucedió con 9 por ciento, cada uno, de los carcinomas del ovario y del colon. Parece, pues, que ciertos asientos de tumores primarios como son la vejiga, el útero, el aparato gastrointestinal y el ovario, son más sus-

ceptibles de provocar metástasis óseas que lo que se cree generalmente.

Las cifras tabuladas de series autópsicas en la literatura muestran que la incidencia observada por el A. es algo más alta que aquellas. No obstante, parece que la misma puede constituir el mínimo y que la frecuencia real de las metástasis esqueléticas quizás sea considerablemente mayor.

Trátase también de correlacionar la incidencia de metástasis óseas descubierta en la autopsia con la calculada para la población en general. Sin embargo, las cifras obtenidas son puramente hipotéticas.

## Double-Contrast Studies of the Colon with Special Reference to Preparation and Fictitious Polyps<sup>1</sup>

C. W. YATES, M.D.,<sup>2</sup> R. D. MORETON, M.D., and E. M. COOPER, M.D.<sup>3</sup>

**I**N OUR WORK WITH the double-contrast method for roentgenologic studies of the colon, we were impressed by the large number of repeated examinations necessary to differentiate between organic and "fictitious" polyps. A search for the causes and elimination of these fictitious shadows has focused our attention primarily on the best method of cleansing the bowel for the examination, the effect of meals prior to the examination, the effect of previous laxative habits, and the effect, if any, of the type of lubricant used on the enema tip.

In order to arrive at a common denominator with reference to meals, 220 colon studies were made after the patient had had supper and no breakfast prior to the examination at 8 A.M., and 534 were made with the same preparation, but no supper and a light breakfast. It was found that 51 per cent of the double-contrast studies had to be repeated for those patients who were allowed to eat supper; while only 21.7 per cent of those patients who had no supper but ate breakfast required re-examination. Consequently, all further studies were made with the patients omitting supper but having a light breakfast prior to reporting for examination at 8 A.M.

To determine the value of different types of enema, hypertonic saline, normal saline, tap water, and soapsuds enemas were used two hours prior to examination time, following the same laxative in all cases, given the preceding evening. Results were also observed following the use of a laxative only. Hypertonic saline enemas were found to be unsatisfactory, as practically every patient retained too much fluid in the colon to allow adherence of the barium suspension to the bowel wall. The same difficulty was encountered in a large per-

centage of the 93 patients receiving normal saline enemas, and to a lesser degree in the 157 given plain water enemas. The best results were obtained with castile soapsuds enemas, in 164 patients. In 56 cases laxatives only were used. It was found that approximately 41 per cent of this group had retained fecal material in the descending colon and sigmoid in sufficient amounts to interfere with good studies.

To determine the possibility of the enema-tip lubricant acting as a source of "fictitious polyps," 349 examinations were made in which the patient was instructed to use only soap as a lubricant. This resulted in a significant reduction in the number of examinations showing "fictitious polyps" as compared with the results when a non-water-soluble lubricant was used.

A comparative study of three laxatives—castor oil (2 oz.), compound licorice powder (5 drachms), and phenolphthalein (3 gr.)—was carried out (Chart I). Otherwise the preparation instructions were identical. Of the 530 patients taking castor oil, 30 per cent were considered incompletely prepared, and 21.7 per cent of these required re-examination due to fictitious polyps. Of the 84 patients taking licorice powder, 40 per cent were considered incompletely prepared; 27.5 per cent having double-contrast study had to be re-examined, and 30 per cent stated that they had no bowel movement before taking an enema. Examination of the 154 patients using phenolphthalein showed 31 per cent poorly prepared; 26 per cent having double-contrast study had to be re-examined.

From the above preliminary studies, it was felt that the time of pre-examination meals, the use and type of enema, and the use of a non-water soluble lubricant on the

<sup>1</sup> From the Scott & White Clinic, Temple, Texas. Accepted for publication in December 1949.

<sup>2</sup> Former Fellow in Radiology, Scott & White Clinic, Temple, Texas.

<sup>3</sup> Fellow in Radiology, Scott & White Clinic, Temple, Texas.

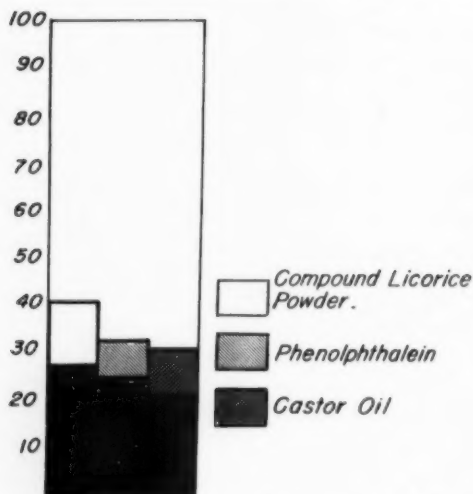


Chart I. Comparison of effectiveness of laxatives. Complete bar represents percentage of patients incompletely prepared, and dark area the percentage needing re-examination.

enema tip have a definite relationship to the state of cleanliness of the bowel and to the number of "fictitious polyps" visualized on double-contrast examination. Castor oil, phenolphthalein, and compound licorice powder were found to be proper laxatives in the order listed. It was concluded that the best results were obtained with the following regime: (1) a laxative, with no supper on the evening prior to the examination; (2) small castile soapsuds enemas two hours prior to examination time, and a small breakfast; (3) enema-tip lubrication with a water-soluble substance.

A study was also made to determine the influence of routine bowel habits on preparation. For this purpose, 888 colon studies were made with detailed notes concerning the patient's previous laxative and enema habits, adherence to instructions, number of bowel movements from the laxative prescribed, and foreign material in the bowel at time of examination. From this group, 100 studies were discarded because of failure to follow instructions.

The routine preparation outlined above was observed in conjunction with the following laxatives or combination of laxatives: (1) 1 oz. castor oil; (2) 2 oz. castor oil;

(3) 1 oz. castor oil and no grease on enema tip for preparation or examination; (4) 1 oz. castor oil, bile salts, no grease; (5) 2 oz. castor oil, bile salts, no grease; (6) 2 oz. castor oil, no grease; (7) 5 gr. phenolphthalein with ice water given directly following stomach examination; (8) 1 oz. castor oil, 3 gr. phenolphthalein given three hours previously.

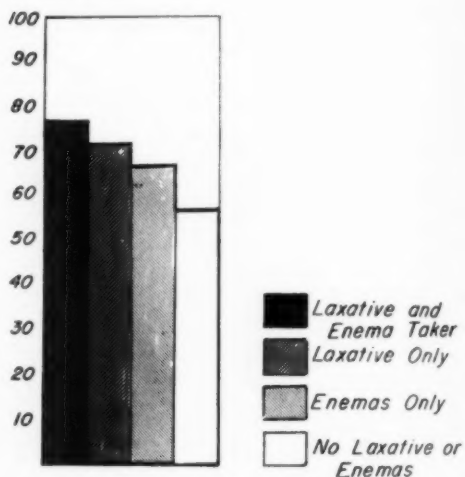


Chart II. Percentage of patients having residual barium in the bowel in relation to routine laxative and enema habits.

In order to have something definite upon which to base our observations, it was decided to accept for this study only those patients who had been given barium by mouth for stomach examination on the afternoon prior to the colon examination. Thus, this part of the study was based on 480 patients, of whom 272 were female and 208 male. It was found that 62.5 per cent of the women and 59.6 per cent of the men had residual barium in the bowel.

The routine laxative and enema habits of the patients seemed to have a very definite effect on the quality of preparation secured (Chart II). Fifty-two gave a history of taking both enemas and laxatives regularly, and of these, 76.9 per cent had residual barium in the colon. Of the 113 patients regularly taking laxatives only, 71.1 per cent showed barium in the colon prior to examination; of the 33 taking

enemas regularly, 66.6 per cent had residual barium; and of those having no laxative or enema habit, only 56.6 per cent (based on all types of preparation) had residual barium in the bowel.

Analysis of various combinations for preparation also showed great variation in some instances (Chart III). Sixty-seven patients took 2 oz. of castor oil, and of this

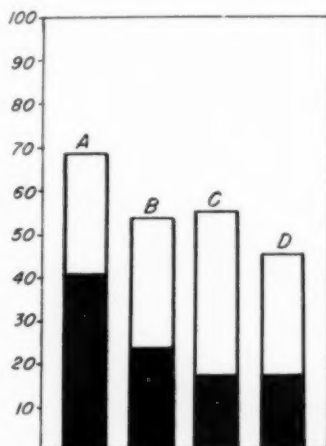


Chart III. Percentage of retained barium in patients after various preparations. Dark area represents that portion of each group needing re-examination either as a result of poor preparation or "fictitious polyps." A. 5 gr. phenolphthalein. B. 2 oz. castor oil. C. 1 oz. castor oil. D. 3 gr. phenolphthalein and 1 oz. castor oil.

group 55.2 per cent had residual barium in the colon; 23.8 per cent were considered poorly prepared, either because the barium was not just in the cecum but was scattered through the colon, or because the patient needed re-examination on account of fictitious polyps. Of the 133 patients taking 1 oz. of castor oil, 55.6 per cent had residual barium in the colon; 17.1 per cent of these were found to have unsatisfactory examinations. Thirty-four patients took bile salts three hours before taking 2 oz. of castor oil, and 58.8 per cent of this group had residual barium; in 23.5 per cent of these the examination was considered unsatisfactory. Forty-three patients were examined following administration of bile salts and 1 oz. of castor oil. Of these, 62.7 per cent showed residual barium, with 25.5

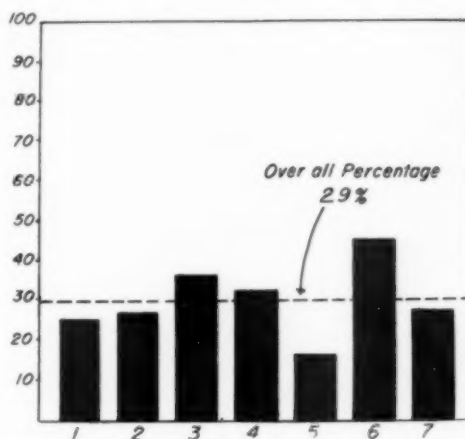


Chart IV. Percentage of fictitious polyps found after employment of various preparations. 1. 1 oz. castor oil with I-X. barium. 2. 1 oz. castor oil with Stabarium. 3. 2 oz. castor oil. 4. 2 oz. castor oil following bile salts. 5. 1 oz. castor oil after bile salts. 6. 5 gr. phenolphthalein. 7. 1 oz. castor oil following 3 gr. phenolphthalein.

per cent of these needing re-examination. Eighty-two patients drank a glass of ice water immediately following their stomach examination and then took one ounce of oil in the evening; 68.3 per cent had residual barium, and of these, 30.4 per cent had unsatisfactory examinations. Thirty-five of the patients examined took 3 gr. of phenolphthalein at 3 P.M. and 1 oz. of castor oil three hours later; 48.5 per cent of this group had residual barium, and 17 per cent of these needed re-examination. Of the 44 patients taking 5 gr. of phenolphthalein, 75 per cent had residual barium in the colon and in 40.9 per cent of these examination was unsatisfactory. Forty-two patients drank a tumbler of ice water immediately after their stomach examination and later took 5 gr. of phenolphthalein. Examination revealed that 71.2 per cent of these had residual barium the next morning, with 47.2 per cent needing re-examination.

Because of the varying number of fictitious polyps seen in patients having essentially the same preparation (Chart IV), the possibility that many of the uniformly rounded, clear shadows were due to air bubbles was also considered. A barium



Fig. 1. Double-contrast examination in patient using hypertonic saline enemas. Note inability of barium to adhere to colon wall.

was used containing an agent to increase the surface tension of such "air bubbles," and in 50 double-contrast studies of the colon this type of shadow was not found. This confirmed the belief that practically all such shadows are due to air bubbles. This mixture was not preferred for routine use, however, because the agent used to increase surface tension caused precipitation of the barium, thickening of solution, etc., making the examination more difficult. It was also found that these shadows could be increased by pumping air slowly through a column of barium. This experiment showed, also, that by rolling the patient over after filling the colon with air and moving the column of barium, many of these bubbles could be broken by the impact of the heavier column.

The question then arose as to what fictitious polyps really were. Various materials were injected into an artificial rubber colon and air films were made of the simulated colon in order to study the question more thoroughly. From this experiment it was found that fictitious polyps

are the result of various fecal particles, oil globules, such as undigested castor oil or mineral oil, non-water-soluble grease introduced on proctoscope and enema tips, and air bubbles coated with barium.

#### DISCUSSION

The better results obtained with castor oil when the patient is not allowed supper, but a small breakfast, bear out a statement by Goodman and Gilman that this laxative acts as do other fatty substances and retards gastric emptying time. As pointed out by Garland, allowing the patient to have even a small breakfast reduces the efficiency of preparation, especially in the region of the cecum, because of the gastrocolic reflex. For this reason, when patients are examined primarily to check the cecum, they are requested to omit breakfast until after the examination. The patient's frame of mind and disposition are much better if he is allowed to have toast and coffee, and the examination is made easier in many instances.

The hypertonic saline enema increases the fluid in the bowel. It dilutes the solution and makes the bowel wall too wet for adherence of the barium and therefore causes an unsatisfactory examination (Fig. 1). The normal saline and water enemas do the same thing to a lesser degree, while soapsuds has just enough irritant effect to make the colon contract and leaves the bowel wall more receptive for the barium solution. The enemas should be small (approximately 500 c.c.; not in excess of one quart), for if too much fluid is used, some will be retained in the sigmoid colon and make examination of this part unsatisfactory (Fig. 2).

Two ounces of castor oil has been used routinely for many years. Goodman and Gilman point out that the purgative dose of this drug is 15 to 30 c.c. and that any amount over this is expelled as undigested oil. For this reason, 1 oz. of castor oil was tried and it was found that the average number of bowel movements following this amount was the same as in patients taking 2 oz. Also the number of oil globules, and

certainly the possibility of visualizing these on double-contrast examination, were reduced.

Bile salts (Bilron) were given three hours before the castor oil with the hope that this would help in digesting the fatty acid globules of the oil and therefore reduce the number of fictitious polyps demonstrated on the double-contrast film. It did not reduce their occurrence sufficiently to warrant its routine use.

Ice water was given immediately after the stomach examination with the idea of increasing small bowel peristalsis and causing more rapid emptying of the barium. This did not aid materially, because our patients have lunch immediately following the stomach examinations and this probably furnishes the same stimulus.

Phenolphthalein in the form of phenolax (U.S.P.), as well as compound licorice powder, was used with the hope of finding a laxative that properly cleansed the large bowel and yet left no oil residue. These did not prove as satisfactory as castor oil. The combination of phenolphthalein and castor oil, giving both a small and large bowel stimulus, seemed to produce the best results.

The investigation of the patient's laxative and enema habits was decided upon because it was felt that the bowel which was constantly stimulated by enemas and laxatives would have lost much physiological tone and would be less likely to respond to similar materials used in preparation for double-contrast study. This was found to be true and it was further demonstrated that these patients did not evacuate as completely as those not accustomed to taking enemas and laxatives, with the result that the post-evacuation films were of inferior quality.

#### CONCLUSIONS

(1) Better preparation for double-contrast roentgenologic study of the colon is obtained by allowing the patient to have a small breakfast before the examination rather than supper the night before. However, because of the gastrocolic reflex,



Fig. 2. Double-contrast examination in patient having retained fluid in right colon due to too large an enema. Note excellent coating of wall of left colon with barium and unsatisfactory results on the right.

breakfast should be omitted when the primary interest is in studying the cecum.

(2) Castile soapsuds is the preferable enema solution, without the use of grease on the enema tip.

(3) Routine enema and laxative habits have an important bearing on the results obtained from preparation.

(4) Fictitious polyps may be due to fecal material, mineral and vegetable oil globules, non-water-soluble grease, as from enema and proctoscope tips, and air bubbles.

(5) One ounce of castor oil is the best laxative for routine preparation.

(6) The complete preparation schedule now used as a result of this study is:

- (a) Eat no supper on previous day.
- (b) At 6 P.M., take 1 oz. of castor oil, disguised, if preferred, with root beer, etc.

- (c) Beginning at 6 A.M., take three small soapsuds enemas at 15-minute intervals (use soap on enema tip rather than grease).
- (d) Have a small breakfast at 7 A.M.
- (e) Report to X-ray Department for examination at 8 A.M.

NOTE: Thanks to Mr. C. M. Jeffers, pharmacist at this institution, for his help and advice regarding action and dosage of these laxatives, as well as making them available for this study.

## REFERENCES

- GARLAND, L. H.: Personal communication.  
 GOODMAN, L., AND GILMAN, A.: *The Pharmacological Basis of Therapeutics: A Text Book of Pharmacology, Toxicology and Therapeutics for Physicians and Medical Students*. New York, Macmillan Co., 1941.  
 MORETON, R. D., STEVENSON, C. A., AND YATES, C. W.: Fictitious Polyps as Seen in Double-Contrast Studies of the Colon. *Radiology* **53**: 386-393, September 1949.  
 STEVENSON, C. A., MORETON, R. D., AND COOPER, E. M.: Nature of Fictitious Polyps in the Colon. *Am. J. Roentgenol.* **63**: 89-94, January 1950.

506 Hermann Professional Bldg.  
 Houston, Texas.

## SUMARIO

### Estudios de Doble Contraste del Colon con Referencia Particular a la Preparación del Enfermo y los Pólipos Falsos

Los estudios ejecutados con mira a determinar las causas de los resultados poco satisfactorios obtenidos con la técnica de doble contraste en el examen roentgenológico del colon, condujeron a las siguientes conclusiones:

Consíguese mejor preparación para el estudio roentgenológico en doble contraste del colon dejando que el enfermo consuma un pequeño desayuno antes del examen en vez de cena la noche anterior. No obstante, debido al reflejo gastrocólico, hay que omitir el desayuno si lo primordial es estudiar el ciego.

Una solución de jabón de Castilla es la preferible para enema, sin emplear grasa como lubricante.

Los hábitos del enfermo en cuanto a enemas y laxantes guardan una relación importante con los resultados obtenidos con la preparación del mismo, pues los intestinos constantemente estimulados en dicha forma pierden su tonicidad fisiológica, siendo menos probable que respondan a providencias semejantes en la preparación para examen.

Los pólipos falsos pueden deberse a materias fecales, glóbulos de aceite mineral o vegetal, grasa anhidrosoluble, tal como la procedente del extremo de la jeringa o el proctoscopio, o burbujas.

El mejor laxante para la preparación corriente consiste en 30 cc. de aceite de ricino.

El esquema completo que emplean ahora los AA. para preparación a consecuencia de este estudio, es el siguiente:

- (1) Suprímase la cena la noche anterior.
- (2) A las 6 P.M., tómense 30 cc. de aceite de ricino, disfrazando el sabor, si se prefiere, con alguna bebida refrescante, etc.
- (3) Comenzando a las 6 A.M., aplíquense, a plazos de 15 minutos, tres pequeños enemas jabonosos (úsese jabón, más bien que grasa, en la punta de la jeringa).
- (4) Tómese un pequeño desayuno a las 7 A.M.
- (5) Acúdase al Departamento de Rayos X a las 8 A.M. para examen.

# Roentgenographic Findings in Schönlein-Henoch's Purpura

## A Case Report<sup>1</sup>

JOHN S. FETTER, M.D., and WILLIAM L. MILLS, M.D.

Philadelphia, Penna.

PURPURA IS OF two main types, thrombocytopenic and non-thrombocytopenic. Schönlein-Henoch's purpura is an example of the latter. Davis (1) describes it as a condition in which non-traumatic hemorrhage, with or without edema, occurs in the skin or subcutaneous tissues or joints or viscera, or in any combination of these, and in which the blood platelets are normally abundant. The cause of this condition is unknown. In only a small number of cases can allergic factors be demonstrated (2).

It may be a syndrome, and not a disease, representing a non-specific reaction to different factors. One important cause may be a recent infection by hemolytic streptococci (1).

Reimann (3) believes that certain cases of the Schönlein-Henoch syndrome belong to a group of periodic or cyclic diseases. In none of the diseases in this category is the cause known and until the theories propounded are proved, Reimann likes to regard periodic disease as a manifestation of a rhythm of life.

Osler described four types of lesions, all of an exudative character (4).

1. Purpura. This may be simple and edema may be present in the hands and feet.

2. Effusions of serum causing urticarial wheals or angioneurotic edema. Identical attacks of intestinal symptoms are seen in angioneurotic edema (5).

3. Diffuse erythema.

4. Necrotic areas, which may be followed by the formation of bullae or ulcers.

Cecil claims that there are foci of hemorrhage and edema in the gastro-

intestinal tract, causing pain, often colicky, diarrhea, melena, and even intussusception (6). Schönlein-Henoch's purpura rarely causes massive upper gastro-intestinal hemorrhage (7).

Because Schönlein-Henoch's purpura can cause such gross changes in the intestinal tract, it seems strange that these have not been observed roentgenologically, with greater frequency. Whitmore and Peterson (8) were the first to describe the roentgenologic picture. They demonstrated, in a case report, irregularity in the terminal portion of the duodenum and first part of the jejunum. The bowel in these regions was dilated, with irregularities of the mucosal outline, resembling small diverticula or ulcers. The dilated portion of the intestine was about 25 cm. in length. Below this level some of the loops were of normal diameter, others were decreased in size, with no normal mucosal pattern visible. Re-examination six weeks later showed a normal small bowel pattern with normal motility. Kraemer (9) has since reported another case with similar small bowel changes.

## CASE REPORT

On Feb. 16, 1948, J. J. T., a white male physician, age 49, entered Nazareth Hospital, with a presumptive diagnosis of Henoch's purpura. Two weeks before admission vague pains in the lower back occurred, followed in a few days by petechiae on the lower extremities. The past medical history and family history were non-contributory.

The temperature, pulse, and respiration were normal; blood pressure 120/74. The lower abdomen and both legs and forearms were splashed with many purpuric spots. No hematologic cause for the purpura was uncovered after completion of extensive blood examinations. A tourniquet test was positive.

<sup>1</sup> From the Department of Radiology, Nazareth Hospital, Philadelphia 15, Penna. Accepted for publication in January 1950.

During the following few days some of the petechiae coalesced, and epigastric pain became the predominant symptom.

Gradually, over the next five-day period, swelling, pain, and tenderness of the left wrist presented. Meanwhile, the epigastric pain persisted and reached a climax on Feb. 26, when the patient was alarmed by vomiting blood-tinged material. On the same day a roentgen examination demonstrated marked duodenal spasm and irritability. At the beginning of the third portion of the duodenum an area of constrictive obstruction was seen. Dilatation



Fig. 1. Obstruction in third portion of duodenum noted at beginning of first study.

occurred proximal to this. The barium was held here for about twenty minutes (Fig. 1). After the duodenum distal to the site of obstruction was visualized, the mucosal pattern was shown to be distorted by widening and irregular filling of the mucosal folds.

At three hours, the obstruction (Fig. 2) was still seen, but most of the barium had passed through the small bowel, the head of the column having reached the hepatic flexure. The entire small bowel was shown to have an irregular pattern.

During the subsequent week repeated examinations of the peripheral blood again failed to give any clue to the cause of the purpura. Nausea and vomiting continued and loose stools occurred. The stools and vomited material contained blood. The patient refused a barium enema examination. Two new crops of petechiae were noted on March 1 and 6.

Treatment was supportive and on March 6 the



Fig. 2. Evidence of partial obstruction of duodenum at three-hour interval.

patient left the hospital. At home the symptoms, which had subsided, recurred and persisted.

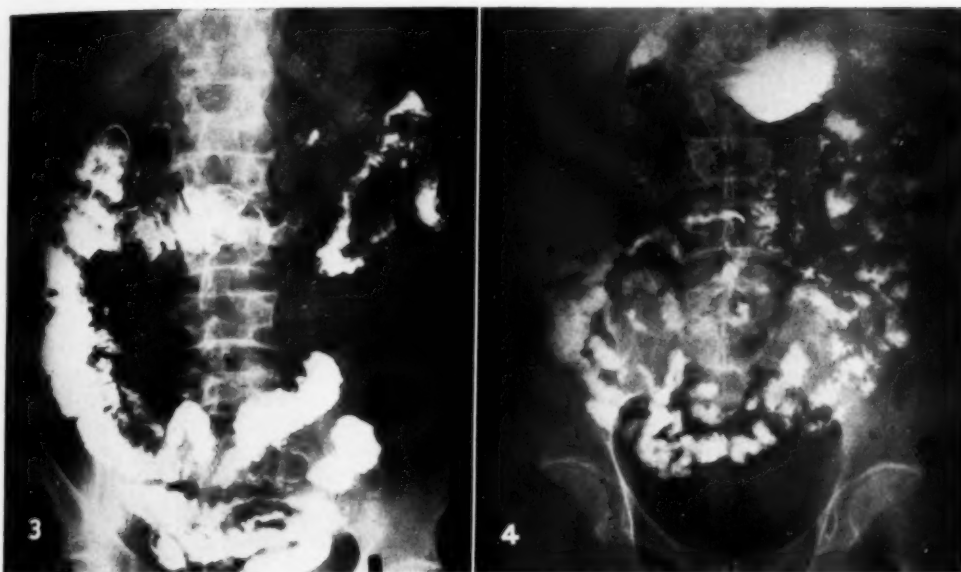
On March 17, 1948, the patient entered another hospital for the same illness. At this time vomiting had ceased and the most troublesome complaint was watery diarrhea. Laboratory examinations further confirmed the original diagnosis.

Through the kindness of Dr. Mary Frances Vastine, we were able to follow the progress of the patient and we have included a reproduction of a roentgenogram obtained by her. There was no evidence of obstruction in the duodenum. The mucosal pattern of the third portion of the duodenum was coarse and irregular. The upper loops of the jejunum appeared nearly normal. A three-hour film showed a few patches of barium in the upper small bowel, with much improvement in the pattern as seen on Feb. 26, 1948. The distal small bowel showed segmentation of the barium with an irregular mucosal pattern (Fig. 3).

Following the patient's second discharge he improved slowly. On May 22, 1948, we examined him again, at which time the mucosal pattern of the duodenum and the rest of the small bowel were normal (Fig. 4). At present, October 1949, he is symptom free and has regained all of his lost weight.

#### SUMMARY

A case of Schönlein-Henoch's purpura with partial obstruction of the third portion of the duodenum and an irregular



Figs. 3 and 4. A three-hour film (Fig. 3) made one month after Figures 1 and 2 shows great improvement. Three months later (Fig. 4) no significant changes remained (three-hour film).

appearance of the small bowel has been presented. Follow-up examinations over a three-month period showed return of the small bowel to normal and disappearance of symptoms. These small bowel changes were demonstrated roentgenologically.

EDITOR'S NOTE: It is of interest that two reports of Schönlein-Henoch's purpura were submitted for publication on the same day. For the other paper, presenting two cases, see page 548.

#### REFERENCES

1. DAVIS, E.: Schönlein-Henoch Syndrome of Vascular Purpura. *Blood* 3: 129-136, February 1948.
2. WINTROBE, M. M.: *Clinical Hematology*. Philadelphia, Lea & Febiger, 2d ed., 1946, p. 627.
3. REIMANN, H. A.: Periodic Disease. Periodic Fever, Periodic Abdominalgia, Cyclic Neutropenia,

Intermittent Arthralgia, Angioneurotic Edema, Anaphylactoid Purpura and Periodic Paralysis. *J. A. M. A.* 141: 175-182, Sept. 17, 1949.

4. OSLER, W.: Visceral Lesions of Purpura and Allied Conditions. *Brit. M. J.* 1: 517-525, March 7, 1914.

5. OSLER, W.: *Principles of Practice of Medicine*, with assistance of Thomas McCrae. New York, D. Appleton & Co., 8th ed., 1909, p. 752.

6. CECIL, RUSSEL, McDERMOTT, W., AND WOLFF, H. G., editors: *Textbook of Medicine*. Philadelphia, W. B. Saunders Co., 7th ed., 1947, p. 1100.

7. BOCKUS, H. L.: *Gastro-Enterology*. Philadelphia, W. B. Saunders Co., 1943, Vol. I, p. 575.

8. WHITMORE, W. H., AND PETERSON, G. M.: Henoch's Purpura: Small Intestinal Changes. Case Report. *Radiology* 46: 373-376, April 1946.

9. KRAEMER, M.: Henoch's Purpura: A Case with Bullous Skin Lesions and Residual Scars, Roentgenologic Considerations. *Gastroenterology* 9: 608-611, November 1947.

Nazareth Hospital  
Philadelphia 15, Penna.

#### SUMARIO

#### Hallazgos Roentgenográficos en la Púrpura de Schönlein-Henoch: Comunicación de Un Caso

El caso descrito es de púrpura de Schönlein-Henoch con oclusión parcial de la tercera porción del duodeno y patrón irregular de todo el intestino delgado. Los exámenes proseguídos durante un período

de tres meses demostraron el retorno del intestino a lo normal y la desaparición de los síntomas. Las alteraciones del intestino delgado eran observables roentgenográficamente.

# Small Intestinal Abnormalities in Anaphylactoid Purpura

## Report of Two Cases<sup>1</sup>

JOSEPH I. ESPOSITO, M.D.

Bridgeport, Conn.

PURPURA IS A MANIFESTATION of pathological bleeding which may occur as the result of various underlying diseases or mechanisms. In general, the bleeding is due either to a deficiency in the clotting mechanism or to an increase in vascular permeability. The purpura which may result from an allergic or anaphylactoid reaction is commonly classified as attributable to an abnormal capillary response (1, 2). The name "Henoch's purpura" has been given to the type associated with gastro-intestinal symptoms, presumably due to an allergic serosanguineous involvement of the intestinal wall. However, other sites, particularly the skin and joints, are frequently involved. Thus, the terms Schönlein-Henoch's syndrome and anaphylactoid purpura are assigned to the exanthem found associated at different times with gastro-intestinal symptoms, joint symptoms, edema of the face and extremities, and nephritis.

Gairdner (3) reviewed 12 cases of "anaphylactoid purpura." He found a "rash" in all, gastro-intestinal symptoms in all but one, and articular symptoms in 10 of the 12. Eight patients passed blood in the stools. The disease is predominantly, but not exclusively, one of childhood and more frequently involves males. Since the gastro-intestinal symptoms are variable and frequently precede the skin eruption, many of the cases are confused with such conditions as appendicitis, ileitis, and intussusception, with frequent resort to unnecessary surgery (4).

Abnormalities in the radiographic appearance of the small intestine occurring in a case of Henoch's purpura were described in 1946 by Whitmore and Peterson

(5). Kraemer (1947) also reported small intestinal changes in a case of Henoch's purpura (6). These cases displayed two common features. First, the radiographic changes were demonstrable before the appearance of purpura on the skin. Second, the small intestine reverted to a normal pattern after the subsidence of symptoms. The two cases of anaphylactoid or Henoch's purpura reported here also demonstrate "pre-exanthematous" abnormal and reversible changes in the small intestine. This report may serve to emphasize the diagnostic importance of small intestinal abnormalities in cases of acute abdominal pain of uncertain etiology.

### CASE REPORTS

CASE I: R. C., Italian male, age 6, was admitted to Danbury Hospital on July 9, 1948, because of generalized abdominal pain, associated with nausea and vomiting, as well as a mild diarrhea. Gross blood had been noted in the stools on the day of admission. During the four preceding days the child had complained of anorexia and occasional abdominal pain of no definite localization. About nine months previously, he had experienced similar abdominal pain of short duration but without melena.

Physical examination on admission was entirely negative. No skin eruptions were noted. Abdominal palpation revealed no localized tenderness, spasm, or masses. The temperature was 100°, pulse 100, respirations 20. The laboratory findings on admission were: hemoglobin 95 per cent; red cells 4,840,000; white cells 14,100, with polymorphonuclears 72 per cent, lymphocytes 21 per cent, eosinophils, 1 per cent, and monocytes 6 per cent; clotting time three minutes; bleeding time one minute. The platelets did not appear unusual. Tests for occult blood in the stools were positive. Urinalysis was negative.

The abdominal pain continued with irregular frequency and intensity. There were, however, no localizing abdominal signs. Penicillin and sedatives were administered daily.

<sup>1</sup> From the Departments of Radiology, Bridgeport and Danbury, Conn., Hospitals. Accepted for publication in January 1950.

On July 13, a routine gastro-intestinal examination was conducted. The esophagus and stomach showed no abnormality, though the stomach emptied slowly. At the four-hour (Fig. 1) interval it still contained considerable barium, although the head of the barium column had progressed to the transverse colon. The visualized loops of jejunum and ileum showed irregularity in the caliber of the lumen. Hypertonic, contracted loops of jejunum were seen. The ileal loops were dilated. Some segmentation was present. The margins of the contracted, hypertonic loops, in particular, showed considerable irregularity, with a loss of mucosal architecture. In some areas, the irregular mucosal outline was suggestive of ulceration. The loops of jejunum, in fact, showed no identifiable mucosal pattern. The impression was that we were dealing with an acute inflammatory enteritis.

On July 15, two days later, the patient became confused and restless. He was unable to sit up and became drowsy and incoherent. Foul-smelling, bloody stools were passed. The temperature rose to 101.4°. On the same day, a paralysis of the right upper extremity became evident. There was a bilateral Babinski reflex. The knee and ankle jerks were absent. The neurological examination was otherwise negative and a lumbar puncture showed no abnormal findings. The next day the fever and paralysis had disappeared. On July 20, an episode of bloody diarrhea occurred. The hemoglobin was 92, the white cell count 16,500.

On July 24, fifteen days after admission, a purpuric eruption was noted over both extremities, groins, buttocks, and in the peri-umbilical region. On July 25, the white cell count was 30,900. Urinalysis (July 26) showed 20 to 30 red blood cells and 75 to 100 white blood cells per high-power field. The stool was positive for blood. The platelet count was 449,300, clotting time three minutes, bleeding time one minute, red cell count 3,430,000. During the next few days occasional pain in the lower extremities was present. On Aug. 6, the eruption had completely disappeared.

A re-examination of the gastro-intestinal tract on Aug. 9 showed essentially normal loops of jejunum; no abnormalities were demonstrated. On Aug. 13, the patient was discharged from the hospital. He had been free of abdominal and extremity pain for several days. Examination of stools showed no evidence of occult blood.

**CASE II:** F. S., Italian male, age 56 years, was admitted to the Bridgeport Hospital Nov. 17, 1946. Four days previous to admission he first experienced a dull pain across the lower abdomen. There was no nausea or vomiting. For the next four days the abdominal pain continued, dull but of sufficient intensity to disturb the patient's sleep. His bowel movements showed no change until the day of admission, when he passed a small, soft stool with no gross blood. There were no urinary symptoms and

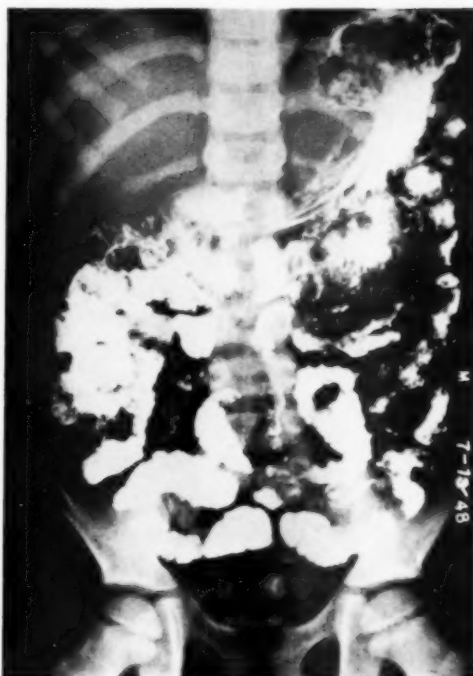


Fig. 1. Case I. Roentgenogram made four hours after barium and water drink, showing gastric residue and abnormality of small intestine. The jejunal loops are narrowed and irregular in outline. Most of the mucosal folds are obliterated. The loops of ileum show dilatation and segmentation.

no apparent fever. No medication had been taken.

The past history was essentially non-contributory; no allergic background was discovered.

Physical examination revealed only slight distention of the abdomen, without local spasm or tenderness. The temperature was 99°, pulse 80, blood pressure 122/84. Blood studies showed: hemoglobin 15.2 gm. (101.3 per cent); red cells 5,230,000; white cells 15,250, with 68 per cent polymorphonuclears, 20 per cent lymphocytes, 8 per cent monocytes, 2 per cent eosinophils, 2 per cent basophils. No platelet count was done but the smears showed the platelets to be normal.

Roentgen examination of the abdomen revealed no abnormalities. Examination by barium enema showed no abnormality of the colon.

The patient was given antispasmodics and Kaomagma and was placed on a low-residue diet, with penicillin, 25,000 units every three hours for three days. On the third day he began to feel relieved of pain and the stools were of normal consistency. A stool specimen showed a highly positive benzidine test for occult blood after a meat-free diet. Urinalysis was essentially negative. On the fifth day, a gastro-intestinal examination was



Fig. 2. Case II. Roentgenogram made one hour after barium and water drink. The distal duodenum and proximal jejunum show deepening and marked widening of the mucosal folds, with some dilatation of the intestine.

done; except for a small hiatus hernia the esophagus and stomach appeared normal. The distal portion of the duodenum, however, and the adjacent loops of jejunum showed markedly widened, edematous mucosal folds. The lumen was dilated. Deep and irregular mucosal outlines were observed (Fig. 2). At the four-hour interval, there was still a small amount of barium in the stomach and some barium was distributed through the transverse colon. Most of the barium, however, remained within the abnormal duodenal and jejunal loops, with two dilated, segmented ileal loops demonstrable. Marked irregularity and widening and deepening of mucosal folds was noted. Along the outer margins of the proximal jejunum were small, discrete barium shadows suggestive of ulcerations (Fig. 3). These findings were interpreted as indicating an enteritis.

On the seventh day, Nov. 25, the patient had been free of abdominal pain for two days, and no signs of abdominal tenderness were found. He was, therefore, discharged to careful observation at home. On Dec. 3, he again saw his physician and exhibited a purpuric rash, which he stated had first appeared on the day of his discharge from the hospital, *i.e.*, about eleven days from the onset of his abdominal symptoms. Numerous small purpuric areas were distributed over both lower and upper extremities, the scrotum, and lower abdomen. A platelet count was not done but again the blood smears showed apparently normal platelets.

The rash disappeared slowly over the next three

weeks. On Jan. 10, 1947, about seven weeks after admission to the hospital, the gastro-intestinal tract was again examined (Fig. 4). A slight tendency to coarsening of the mucosal outlines of small intestinal loops was demonstrable, with slight segmentation, probably indicating some residual disturbance in physiology. However, the duodenal and jejunal loops which previously showed such marked local abnormality now presented a well visualized normal mucosal pattern.



Fig. 3. Case II. Roentgenogram made four hours after barium and water drink. Marked local hypomotility manifested by residual barium in the abnormal duodenal and jejunal loops. Along the outer margin of the proximal jejunum are small, detached barium shadows, suggesting mucosal ulcerations.

#### COMMENT

In his excellent review of the literature on anaphylactoid purpura, Gairdner found only scanty records of the histologic changes in the intestine. However, from the available evidence, he concludes that the more severe intestinal lesions show localized areas of inflammation and necrosis and that the vessels in these areas may show endothelial proliferation, thrombosis, and fibrinoid necrosis. In some cases, the vascular lesions may amount to a necrotizing arteriolitis. The gastro-intestinal symptoms are shown to be the result of serous or sanguineous extravasations into the intestinal wall, pointing to a



Fig. 4. Case II. Roentgenogram made after subsidence of symptoms and eruption. Note the normal mucosal pattern of the distal duodenum and proximal jejunum. There is a minor motor disturbance of more distal small intestine. (Radiopaque medication is seen in the transverse colon.)

vascular origin. Gairdner proposes that the underlying mechanism is probably an antigen-antibody reaction akin to that in anaphylaxis and occurring especially in the endothelium of the small blood vessels of the skin, synovia, intestines, and glomeruli. In Case I, the process had involved the joints and glomeruli, as well as the central nervous system. Wintrobe (7) points out that transient attacks of paresis may occur, as in this patient. The marked localized abnormalities noted radiographically in our two cases may justifiably be attributed to hemorrhages within the mucosal or submucosal layers of the intestines. As stated by Whitmore and Peterson, such hemorrhages would tend to separate patches of mucosa, giving at least the appearance of, if not actual, ulcerations. Apart from these severe local changes, wherein the mucosal folds are obliterated, other, more diffuse, "physiologic" disturbances are manifested throughout the small intestine by segmentation,

dilatation, hypertonicity, and changes in motility. These may represent "reflex" disturbances secondary to the localized mucosal hemorrhages. However, one may postulate that hemorrhages may also occur within the blood vessels of the mesentery supplying the intestine. This would then lead to a neuromuscular derangement which would result in a disordered motor physiology of the small intestine. Differentiation from an acute enteritis is difficult, but Whitmore and Peterson observed that enteritis is more commonly associated with hypermotility than with hypomotility.

#### SUMMARY

Two cases of anaphylactoid purpura or Schönlein-Henoch's purpura are presented. Both patients showed marked abnormalities of the small intestine on roentgen examination. These changes are attributed to hemorrhages into the mucosal layer of the intestine and possibly into the mesentery. In each case, the roentgen changes preceded the appearance of purpuric skin eruptions. After the subsidence of symptoms, the roentgen abnormalities also disappeared.

144 Golden Hill Street  
Bridgeport 3, Conn.

EDITOR'S NOTE: It is of interest that another report of Schönlein-Henoch's purpura was submitted for publication on the same day as this paper. See page 545.

#### REFERENCES

1. FROMMEYER, W. B., AND EPSTEIN, R. D.: Hemorrhagic Diseases. *New England J. Med.* **241**: 700-712, Nov. 3, 1949.
2. HUMBLE, J. G.: Mechanism of Petechial Hemorrhage Formation. *Blood* **4**: 69-75, January 1949.
3. GAIRDNER, D.: Schönlein-Henoch Syndrome. *Quart. J. Med.* **17**: 95-122, April 1948.
4. ALTHAUSEN, T. L., DEAMER, W. C., AND KERR, W. J.: The False "Acute Abdomen"; Henoch's Purpura and Abdominal Allergy. *Ann. Surg.* **106**: 242-251, August 1937.
5. WHITMORE, W. H., AND PETERSON, G. M.: Henoch's Purpura: Small Intestinal Changes. *Case Report. Radiology* **46**: 373-376, April 1946.
6. KRAEMER, M.: Henoch's Purpura: A Case with Bullous Skin Lesions and Residual Scars, Roentgenologic Considerations. *Gastroenterology* **9**: 608-611, November 1947.
7. WINTROBE, M. M.: In the *Cyclopedia of Medicine, Surgery, and Specialties*. Philadelphia, F. A. Davis Co., 1945, Vol. 2, pp. 822-825.

(Para el sumario en español, véase la página siguiente.)

## SUMARIO

**Anomalías del Intestino Delgado en la Púrpura Anafilactoidea.****Presentación de Dos Casos**

Los dos casos presentados son de púrpura anafilactoidea o púrpura de Schönlein-Henoch. El examen roentgenológico reveló en ambos enfermos notables anomalías del intestino delgado. Esas alteraciones se imputan a hemorragia en la mu-

cosa intestinal y posiblemente en el mesenterio. En ambos casos, las alteraciones roentgenológicas precedieron la aparición de las erupciones purpúricas. Después de ceder los síntomas, desaparecieron las anomalías roentgenológicas.



## Cortical Fissuring in Osteomyelitis Complicating Sickie-Cell Anemia<sup>1</sup>

RUSSELL WIGH, M.D., and HARVEY J. THOMPSON, JR., M.D.

Philadelphia, Penna.

ALTHOUGH the roentgen characteristics of sickle-cell anemia changes in bone are well known and even classified (5), the modifications that this disease as an underlying factor may cause in the evolution of superimposed lesions have not been discussed. That osteomyelitis in patients with sickle-cell anemia may produce an unusual roentgen finding is suggested by the following case of *B. paratyphosus B* infection.

While bone infections in patients with sickle-cell anemia are relatively more common than in the normal individual (2), no analysis of the roentgen manifestations could be found.

Paratyphoid osteomyelitis, the second factor in the case to be reported here, is a comparatively rare entity. In 1934, Veal and McPetridge (7) added 2 cases to the 18 which they found in the world literature. Three additional cases have been described in American reports since then (1, 3, 4). Only one published case of *B. paratyphosus B* osteomyelitis complicating sickle-cell anemia was found (1). None of the roentgenologic descriptions in these reports included the change which is to be described in our case.

### CASE REPORT

A 14-year-old colored boy was admitted complaining of headache, anorexia, nausea, vomiting, and a single episode of epistaxis occurring on the previous day. The onset of acute symptoms began five days prior to admission. During the previous four-year period the patient had had three admissions to Jefferson Hospital, his major complaint having been jaundice. Marked red blood cell sickling and anemia had been observed each time. Multiple transfusions were given during each of these periods of hospitalization.

The positive physical findings at this fourth ad-

mission were bilateral exophthalmos, icteric sclerae, and a soft mitral systolic murmur. The liver and spleen were not palpable.

Laboratory examination revealed a severe anemia; the hemoglobin value ranged between 52 and 64 per cent, and the red cell count between 1,500,000 and 3,200,000. There was a relative leukocytosis. Sickling was pronounced.

The day following admission the patient's temperature had risen to 104° F. For the next week he complained of increasingly severe joint pains, particularly about the knees, and also muscular pains in the legs. Two weeks after admission the temperature had risen to 105° F. and there was exquisite tenderness over both tibiae. The temperature continued between 103 and 104° F., and the patient complained continually of the pains in his knees and legs and in all of the joints. During this period three blood transfusions had been administered; the hemoglobin value was 49 per cent and the red cell count 2,500,000. A leukocytosis of 18,300 cells was found, with a predominance of polymorphonuclears.

After five weeks of hospitalization, an area of tenderness, redness, and swelling over the upper anterior aspect of the right tibia was noted. *B. paratyphosus B* was cultured from material aspirated from this soft-tissue abscess on two occasions. Roentgenologically the source was shown to be an osteomyelitis in the tibia. At that time a skeletal survey indicated the presence of multiple inflammatory lesions.

Both aureomycin and streptomycin therapy were given, although not concomitantly, over a period of twenty-four days. Clinical improvement was progressive, but rather slow. A draining sinus developed in the soft tissues over the aspirated site.

At the end of fifteen weeks the patient was discharged to the Out-Patient Department, and was followed for four months, during which time progress roentgenograms demonstrated complete regression of the several areas of osteomyelitis with the exception of a chronic isolated focus in the upper portion of the right tibia. This continued to discharge through a sinus tract to the skin.

### ROENTGENOLOGIC FINDINGS

Roentgenograms of the skull, chest, pelvis, spine, and long bones of this patient

<sup>1</sup> From the Department of Radiology, Dr. Paul C. Swenson, Director, and the Department of Pediatrics, Service of Dr. Edward L. Bauer, Jefferson Medical College Hospital, Philadelphia, Penna. Accepted for publication in January 1950.

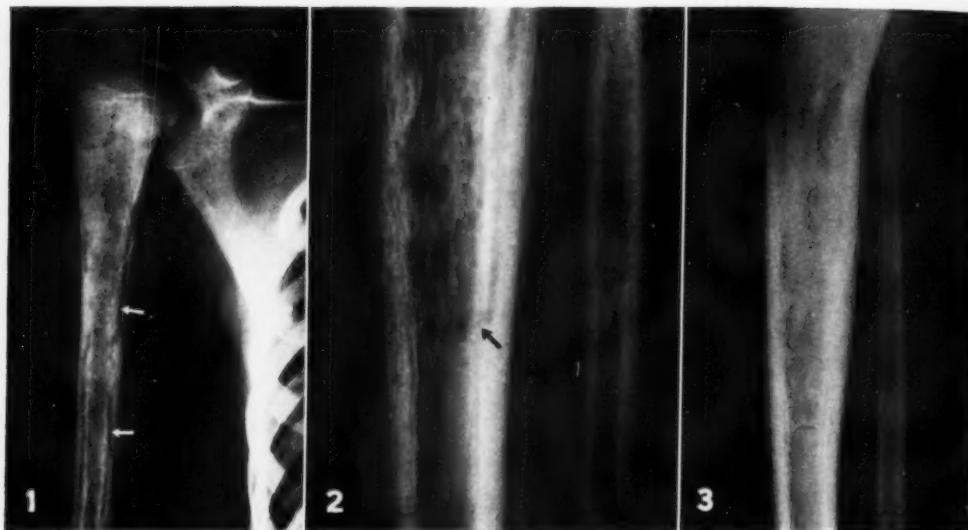


Fig. 1. Arrows point to a fissure. Note that it lies between two layers of split cortex.

Fig. 2. Arrow points to intraosseous tract from area of medullary osteomyelitis to the intracortical fissure in the left tibia.

Fig. 3. Appearance of left tibia after four months. Fissuring is no longer apparent.

had been made during previous admissions. Slight trabecular coarsening in the flat bones and in the spine was present, and there were areas of minimal cortical thickening in the left radius, left ulna, and right fibula.

Early in the present admission, a bone survey demonstrated thickening also of the shafts of the right radius and ulna, both tibiae, and the left femur. An irregular radiotranslucent defect was present in the left femur, and this was considered to be the residue of an uncalcified bone infarct. Since the original spine examinations, made four years previously, some of the vertebral bodies showed a tendency toward biconcavity due to demineralization.

Roentgenograms of the extremities made at the time the abscess first became clinically apparent demonstrated areas of osteomyelitis in all long bones except the femora. The usual destructive features of medullary infection predominated, but periostitis was present in several regions. The diaphyses were infected initially rather than the juxtaepiphyseal regions. The distinctive feature which made the response unusual was the presence of linear intra-

cortical fissuring paralleling the shaft, adjacent to the medullary involvement (Fig. 1). This occurred in six of the ten bones with osteomyelitis. The length of the fissuring was the same as the extent of the medullary disease. The width of the radiotranslucent lines varied from a fraction of a millimeter to 3.0 mm. and was usually thickest near the mid-portion. The margins of the defect were irregular and suggested a tract of infection. In all the bones exhibiting this change there seemed to be short intraosseous sinus tracts between the obvious medullary infection and the cortical fissure (Fig. 2). The communication could always be noticed at one end of the fissure and in some instances it existed at both ends. In no case did the fissure seem to end subperiosteally, although subroentgen communications may have existed. Roentgenograms made in more than one plane indicated that the fissure never extended completely circumferentially around the shaft.

The fissuring was clearly defined as lying between cortex and endosteal limits; it did not represent uncalcified matrix between new subperiosteal bone and cortex. This

was most readily evident when areas of subperiosteal new bone were present external to the periphery of the split cortex.

The compact bone was actually thicker during the phase of fissuring than prior to the infection, since it consisted of the split cortical layers and the intracortical osteitis.

Healing of the intracortical lesions paralleled that of the intramedullary lesions in time sequence. New lime deposits bridged the fissures. Thickening of the shafts of all the bones infected was present. In most instances this resulted not only from the new subperiosteal bone formation, now indistinguishable from the original cortex, but also from endosteal new bone with concomitant narrowing of the medulla. Sequestration and involucrum formation did not occur. In the right tibia a chronic abscess is still present and continues to drain. After four months of follow-up, there is no residual evidence of the cortical fissuring. (Fig. 3).

#### DISCUSSION

Most authors (1, 4, 6, 7) describe the osteomyelitis due to *B. paratyphosus B* as being more frequently diaphyseal than metaphyseal in position, and the present case accords with this observation. The cortical fissuring, however, since it has not been described in instances of paratyphoid osteomyelitis occurring in otherwise normal bone, would appear to be due to the underlying factor of a bony abnormality related to the sickle-cell anemia.

One can only theorize as to the basic mechanism. It may be that loose spongy bone which is dispersed through compact bone during growth is not completely organized into an adult type in these patients. Under these conditions, spongy pathways which are not roentgenologically detectable may exist and permit infection to travel more readily along such cortical bone areas than in the normal patient.

There was no opportunity to examine the bone histologically, and no microscopic descriptions of intracortical bone findings or histochemical analyses in sickle-cell anemia were discovered in the literature.

If fissuring occurs in other cases of osteomyelitis complicating sickle-cell anemia, it could indicate the presence of a faulty structural or chemical factor in the compact bone of these patients. Biological analyses of cortical bone in sickle-cell anemia should increase the knowledge concerning this widespread disease.

#### SUMMARY

1. A case of *B. paratyphosus B* osteomyelitis in a patient with sickle-cell anemia is reported.

2. An unusual roentgen change consisting of intracortical fissuring in the areas of osteomyelitis is described. This modification of the usual findings in osteomyelitis is considered as due to roentgenographically imperceptible changes in compact bone due to the sickle-cell anemia.

3. When such fissuring is noticed in cases of infections in bone, perhaps the presence of an underlying general disease process may be implied.

Jefferson Medical College Hospital  
Philadelphia 7, Penna.

#### REFERENCES

1. BURCH, J. E.: Paratyphoid Osteomyelitis. A Case Report. South. M. J. 42: 138-139, February 1949.
2. DIGGS, L. W., PULLIAM, H. N., AND KING, J. C.: Bone Changes in Sickle Cell Anemia. South. M. J. 30: 249-258, March 1937.
3. JETTER, W. W.: Paratyphoid Fever Complicated by Multiple Foci of Osteomyelitis. Am. J. Dis. Child. 56: 846-851, October 1938.
4. MACDONALD, A.: Paratyphoid Abscess: Recovery of the Organism from Bone-Marrow. Lancet 1: 174-175, Feb. 8, 1941.
5. MACHT, S. H., AND ROMAN, P. W.: Radiologic Changes in Sickle-Cell Anemia. Radiology 51: 697-707, November 1948.
6. VEAL, J. R.: Typhoid and Paratyphoid Osteomyelitis. Am. J. Surg. 43: 594-597, February 1939.
7. VEAL, J. R., AND McFETRIDGE, E. M.: Paratyphoid Osteomyelitis. Report of Two Additional Cases. J. Bone & Joint Surg. 16: 445-450, April 1934.

(Para el sumario en español, véase la página siguiente.)

## SUMARIO

**Fisuras Corticales en la Osteomielitis que Complica la Drepanocitemia**

El caso comunicado es de osteomielitis debida al *B. paratyphosus* B en un enfermo con anemia por células falciformes. Un extraño hallazgo roentgenológico en este caso consistió en la existencia de fisuras lineales intracorticales en las zonas de osteomielitis coincidiendo con las de invasión medular. Entre la manifiesta infección medular y la fisura cortical había un breve trayecto fistuloso intraóseo. La cicatrización de las lesiones intracorticales se con-

formó a la de las lesiones intramedulares.

Considérase que esta modificación de los habituales hallazgos en la osteomielitis es debida a alteraciones roentgenográficamente imperceptibles producidas por la drepanocitemia en el hueso compacto.

Cuando se observan tales fisuras en casos de infección ósea, tal vez denoten la presencia de un subyacente proceso patológico general.



## Effects of Internal Irradiation of Mice With $P^{32}$

Part II: Gonads, Kidneys, Adrenal Glands, Digestive Tract, Spinal Cord, Lungs, and Liver<sup>1</sup>

SHIELDS WARREN, M.D., JANE C. MacMILLAN, M.D., and FRANK J. DIXON, M.D.

Boston, Mass.

A STUDY HAS BEEN made of the histologic damage suffered by a series of mice injected with 25  $\mu$ c., 250  $\mu$ c., and 2 mc. of  $P^{32}$ . Part I (7) dealt with the effects on the spleen, lymph nodes, thymus, bone, and bone marrow. Part II will describe changes in the ovaries, testes, kidneys, adrenal glands, digestive tract, spinal cord, lungs, and liver.

begins with the germinal epithelial cells rounding up and dipping beneath the tunica albuginea, thereby giving rise to an epithelial bud or pearl (Fig. 1). This bud becomes a primordial follicle (Fig. 3), then a primary follicle (Fig. 2), which is composed of a primary oocyte surrounded by a single layer of cuboidal follicular cells. When the follicle develops an an-

TABLE I. OVARIAN STRUCTURES POST-IRRADIATION. AVERAGES TAKEN OF 82 OVARIES

Number of Animals	Dose	Time Post-Injection	Relative Ovary Size	Number of Corpora Lutea	Pearls and Buds	Primary Follicles	Average Number of Ova per Follicle	Secondary Follicles	Average Number of Ova per Follicle
5	Control	.....	5.6	1.8	5	15	13.1	11.0	1.1
10	25 $\mu$ c.	10 days	4.5	2.2	0	7.2	2.5	14.5	1.5
2	25 $\mu$ c.	84 days	5.0	1.5	5.1	8.4	0	24	Few
10	250 $\mu$ c.	10 days	4.5	1.6	1.5	6.5	0.7	15	2.5
6	250 $\mu$ c.	10-20 days	3.5	1.4	4.7	11.8	0.1	8.6	1.1
2	250 $\mu$ c.	50 days	5.0	9.0	5.1	19.0	0	19.0	5.1
6	2 mc.	5 days	2.5	0.3	1.3	8.5	0.7	7.0	0.5

### OVARIES

Previous studies by other workers on internal irradiation with  $P^{32}$  have been scanty in regard to ovarian effects. Therefore, our observations were made as elaborate as feasible. It seemed that the examination of several levels of a large number of ovaries and a still greater number of different component structures yielded to a statistical or mathematical approach. The significant data on which conclusions are based are presented in Table I. In addition, average sizes, based on representative cross sections of the ovaries of each dosage group, are shown in Table II.

For the purposes of the following discussion, a short description of ovarian structure may be useful. It has been shown earlier (1, 2) that mouse oogenesis

trium and measures about 400  $\mu$ , it is called a secondary follicle (Fig. 5). With maturity and increased intrafollicular pressure, the follicle ruptures through the tunica albuginea, ovulation is accomplished, and the entire structure gives rise to a corpus luteum. From three to five follicles thus rupture every four or five days in each mouse ovary.

The most spectacular radiation effect was reduction in size of the ovary. This reduction is closely associated with the functional activity of the ovary, since the latter is composed in large part of multiple corpora lutea and numerous follicles varying from 400 to 500  $\mu$  in diameter. In two to three days the ovaries were all reduced to between one-half and four-fifths of normal size by all dosages of radiation used.

<sup>1</sup> From the Laboratory of Pathology of the Harvard Cancer Commission, Harvard Medical School. This work was done under contract from the Office of Naval Research and Atomic Energy Commission. Accepted for publication in November 1949.

The  $P^{32}$  used was supplied by Oak Ridge National Laboratories, Oak Ridge, Tenn.

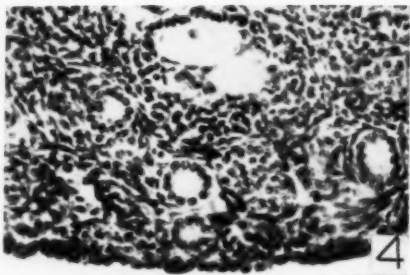
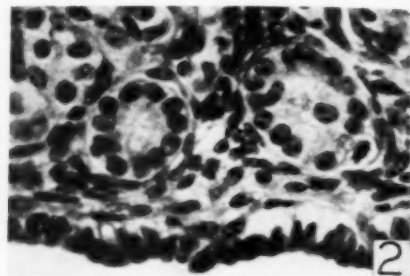
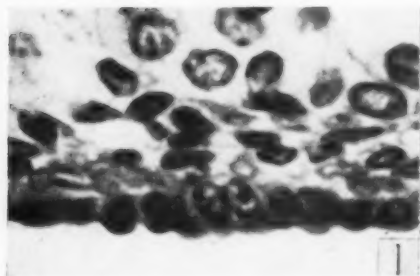


Fig. 1. Germinal epithelial cells differentiating into "pearl" or "bud" before becoming detached from germinal layer. Normal mouse ovary.  $\times 1000$ .

Fig. 2. Primary follicles of normal mouse ovary.  $\times 500$ .

Fig. 3. Primordial follicle and differentiated oocyte of normal mouse.  $\times 500$ .

Fig. 4. Section of ovary of mouse injected with 25  $\mu$ c. of  $P^{32}$  and sacrificed at eighty-four days, showing new growth of primary follicles inward from intact germinal epithelium, but atretic follicles are still seen near top of photograph.  $\times 250$ .

The maximum shrinkage occurred between the tenth and fifteenth day, and full normal size was not regained in any instance, even eighty days after injection. Table II suggests a degenerative effect without regenerative hyperplasia of any integral parts of the ovary up to about two and a half months following injection. Whether this is true or not cannot be said with certainty, but a histologic scrutiny of the radiation effects on the individual structures of the ovaries contributes to the idea.

Although evidence of pearl formation was completely absent in the germinal epithelium ten days after injection of the two larger doses, buds or pearls reappeared in normal numbers and sizes by fifteen to twenty days after injection (Table I). Differentiation to oocytes within the germinal epithelial layer was not found after doses of 250  $\mu$ c. and 2 mc. This is taken to indicate diminished frequency rather than absence of oogenesis. No distinct cyto-

logic effects of irradiation could be noted in these very young germinal forms described above. The effects of irradiation on the primary follicle, however, were quite distinct. The follicular cells shrank, became pyknotic (Figs. 11 and 12), and became detached from the thecal cells, to float free in the follicular cavity. While normally the oocyte is observed in nine-tenths of control follicles, it was not seen so frequently after irradiation. There was marked vacuolization developing within the cytoplasm and the nucleus. The nucleus assumed a wrinkled, irregular appearance, and finally shrank and almost disappeared, leaving a few reddish granules within a hyaline-like nuclear membrane (Fig. 14). The primary effect was disintegration without amitotic progression in ova of this size. It should be noted that normally primordial follicles do not undergo atresia in such quantities as they did following irradiation.

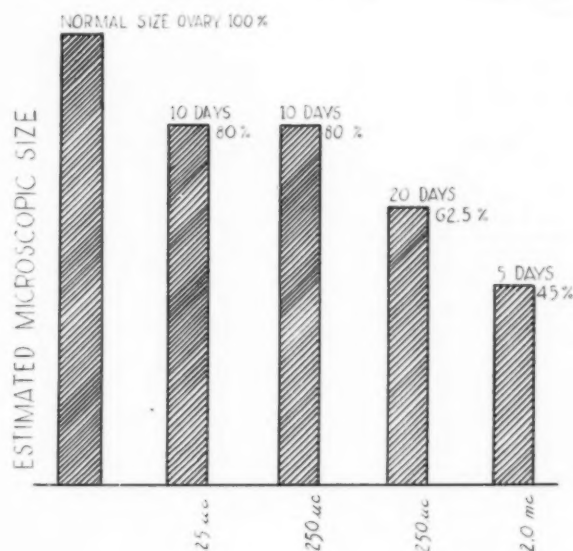
Whereas the degenerative changes described above affected the primary follicles so that at the end of ten days they were seen in only half of their normal number, the secondary follicles at ten days were seen in increased numbers. This is best interpreted as an interference with maturation at this stage. The recognizable onset of slow atresia in 50 to 60 per cent of the follicles at ten days increased with time, until at ninety days 90 per cent of the total follicles were atretic. This was particu-

were phagocytized by polymorphonuclear leukocytes. Eventually this process affected all granulosa cells within a follicle; the empty cavity shrank, only a few fragmentary remains of the ovum persisting.

The early degenerative changes in the ovum appeared almost simultaneously and were many and varied. Four days after irradiation, pre-ovulatory maturation spindles were noted (Figs. 9, 10). These changes could be associated with the early onset of atresia in a subovulatory follicle (5).

TABLE II

### REDUCTION OF OVARIAN SIZE WITH $P^{32}$ INJECTION



larly true of the larger follicles, which have been observed to be destroyed most readily (3). The smaller follicles, with only two to four granulosa-cell layers, appeared more resistant to  $P^{32}$  (Fig. 5).

Histologic effects of radiation seen in the secondary follicles resembled normal atresia. All evidence of mitotic division in the granulosa layers ceased. The earliest visible damage consisted of pyknotic and karyolytic nuclear changes affecting the innermost granulosa cells. Later, chromatolysis of the same cells occurred, with fragmented particles floating in the ovum cavity, which

As has been noted before, the ovum and its remnants persisted longer after irradiation before final disintegration than any of the other follicular structures (Figs. 14, 16). It should be emphasized that qualitatively these varied changes appear in no way peculiar to irradiation injury. Except for the large number of follicles affected, they could resemble the so-called normal atresia or involution of follicles.

With larger doses, the corpora lutea appeared in fewer numbers, as would be expected, with the marked atresia exhibited by most of the larger follicles. The lutein

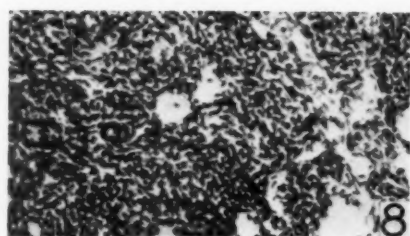
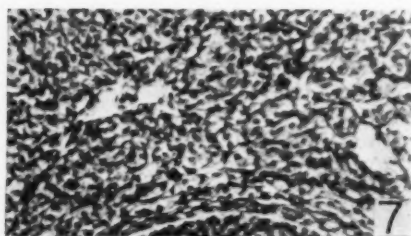
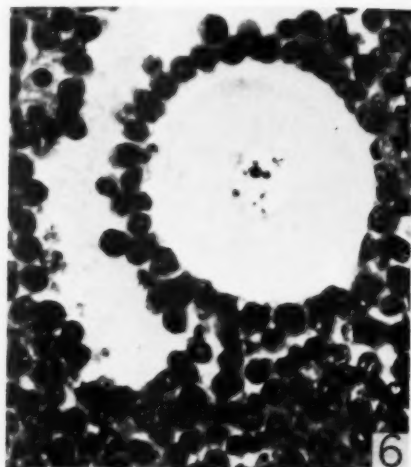
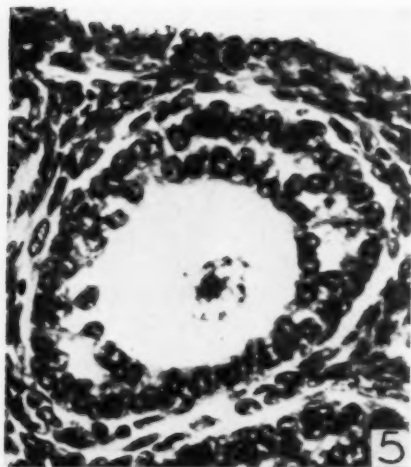


Fig. 5. Secondary follicle of normal mouse ovary.  $\times 500$ .

Fig. 6. Mature-sized follicle (400 micra) of normal mouse ovary showing beginning of early atretic change in oocyte.  $\times 500$ .

Fig. 7. Stroma of normal mouse. Note characteristic arrangement in "cords" resembling embryonal developmental arrangement.  $\times 150$ .

Fig. 8. Stroma of ovary of mouse irradiated with 250  $\mu$ c. of  $P^{32}$ , showing condensation of cellular pattern, and spindle cells predominating.  $\times 150$ .

cells themselves showed no definite irradiation effects except after the lethal 2 mc. dose, when all structural pattern was distorted beyond recognition.

Of all the structures of the ovary, the stroma most nearly approached a characteristic post-irradiation effect, both early and late. Normally the appearance of the adult ovarian stroma retains a modified resemblance to the medullary cords in the embryonic ovary (Fig. 7). The numerous and characteristic interstitial cells are rounded up in columns and mixed with strands of spindle-shaped fibroblasts, giving a pseudo-glandular appearance. After injection of  $P^{32}$ , by contrast, the stromal pattern became fibrotic and condensed, and there was a loss of cytoplasmic substance.

The interstitial cells disappeared or became shrunk and spindle-shaped, with small pyknotic nuclei. (Contrast Figs. 7 and 8). Two to three months later, interstitial "glands" (4) or tissue had developed, filling the entire ovary (Figs. 15-19). It has been noted before in guinea-pigs (6) that, even after minimal radiation injury, there is continued primordial oogenesis, but maturation of the ova never progresses, and the interstitial tissue replaces the follicular structure. The pseudoglandular structure is brought out by a reticular stain (Fig. 15). The exact source of the interstitial tissue is controversial, but it would seem to be originating directly from the theca interna (Fig. 20), and only indirectly from the ovarian stroma.

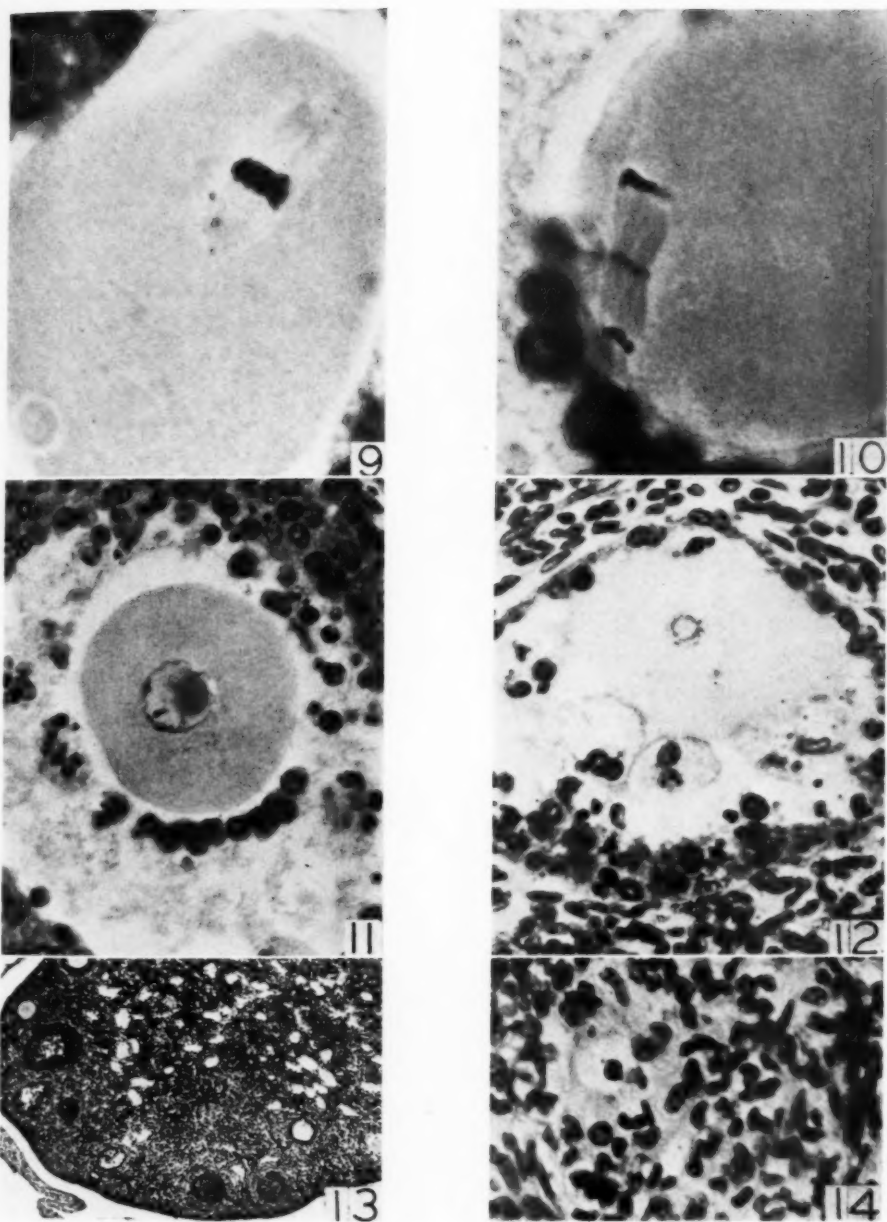


Fig. 9. Premature mitotic division of oocyte in 400-micra graafian follicle of mouse sacrificed twelve days after injection with 250  $\mu$ c. of  $P^{32}$ .  $\times 1000$ .  
 Fig. 10. Diaster formation in oocyte twelve days after injection of 250  $\mu$ c. of  $P^{32}$ .  $\times 1000$ .  
 Fig. 11. Atretic follicle ten days after injection of 250  $\mu$ c. of  $P^{32}$ .  $\times 500$ .  
 Fig. 12. Atretic follicle twenty days after injection of 250  $\mu$ c. of  $P^{32}$ .  $\times 500$ .  
 Fig. 13. Section of ovary from mouse injected with 250  $\mu$ c. of  $P^{32}$  and sacrificed at eleven days, showing follicular atresia in various stages.  $\times 50$ .  
 Fig. 14. Later stage of atresia of graafian follicle than Fig. 13, taken ten days after injection of 250  $\mu$ c. of  $P^{32}$ .  $\times 500$ .

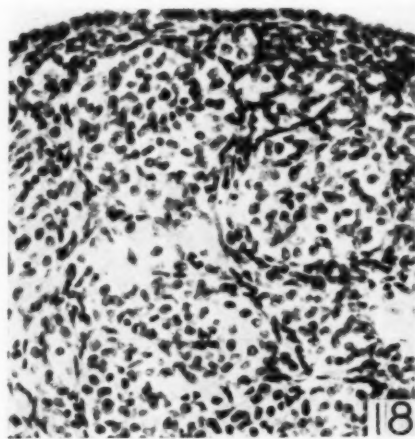
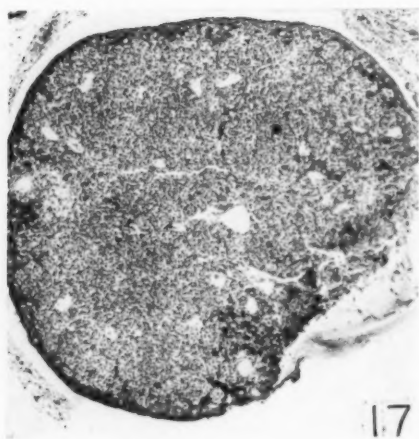
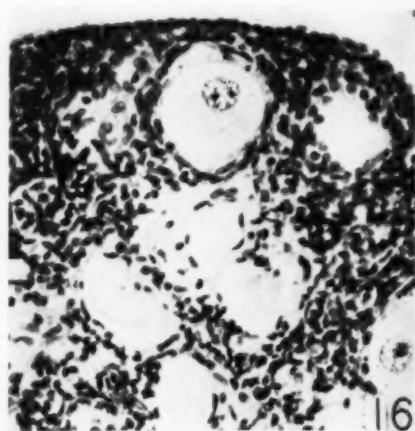
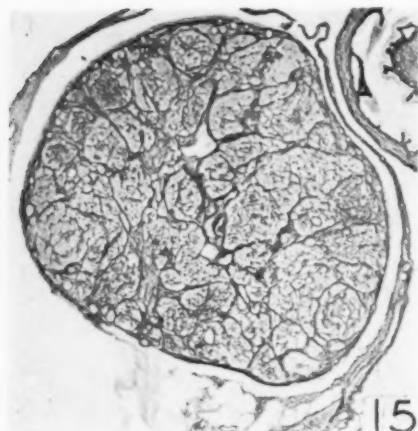


Fig. 15. Reticular stain of mouse ovary, fifty days after injection of 250  $\mu$ c. of  $P^{32}$ , showing pseudo-glandular structure of the interstitial tissue.  $\times 50$ .

Fig. 16. Two persistent oocytes in cleared atretic ovarian follicles, and vacant "spaces" containing hyaline thecal remnants from an animal five days after injection of 2 mc. of  $P^{32}$ .  $\times 250$ .

Fig. 17. Ovary fifty days after injection of 250  $\mu$ c. of  $P^{32}$ , filled with interstitial tissue. Note thickened tunica albuginea. Hematoxylin-eosin stain.  $\times 50$ .

Fig. 18. Enlargement of Fig. 17, showing interstitial tissue replacement of follicles from animal fifty days after injection of 250  $\mu$ c. of  $P^{32}$ .  $\times 250$ .

*Discussion and Summary:* The most characteristic and consistent change in the mouse ovary following injection of  $P^{32}$  is a reduction in total amount of ovarian tissue (see Table II). The factors which contribute most heavily to this are (1) a diminished number of graafian follicles, (2) absence of corpora lutea, and (3) marked condensation of the stroma. This last factor, plus the late development of

interstitial tissue, is considered the most distinctive post-irradiation effect of  $P^{32}$  on the ovary. An absolute sterilizing dose of  $P^{32}$  short of a lethal dose has not been found for mice. Absolute sterilization, we believe, is approached most nearly in those animals living fifty-four days or longer in which there were no corpora lutea. Over 80 per cent of the follicles were undergoing atresia, and ovaries were



Fig. 19. Irradiated ovarian tissue, fifty days after injection of 250  $\mu$ c. of  $P^{32}$ , condensed peripherally by interstitial gland proliferation.  $\times 50$ .

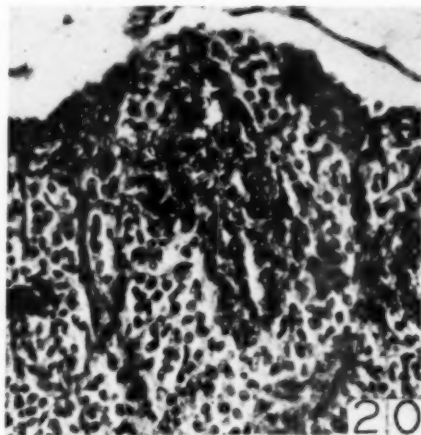


Fig. 20. Follicle showing interstitial tissue replacing follicular structure by four days after injection of 250  $\mu$ c. of  $P^{32}$ .  $\times 250$ .

largely filled by interstitial tissue. Cysts of ovarian structure were not encountered in our study of internal irradiation effects in mice.

#### TESTES

*Spermatogenic Elements:* The 250  $\mu$ c. series of mice affords the best opportunity for study of progressive irradiation changes in the testes. Two days after injection, the only changes in the tubules were increased basophilia and swelling of the nuclei of a few of the sperm. Nine days after injection there was nearly complete loss of the most primitive spermatogenic cells, the spermatogonia, which normally form a single cell layer adjacent to the tubular basement membrane. Only a few hyperchromatic, slightly shrunken cells adjacent to the basement membrane suggested residual spermatogonia. The Sertoli cells, which occur along the basement membrane with the spermatogonia, appeared unaffected (Figs. 22, 26). The primary spermatocytes, forming a layer one or two cells thick, were adjacent to the basement membrane and appeared normal, as did also the secondary spermatocytes. Spermiogenesis appeared normal in about 90 per cent of the tubules, but the remaining 10 per cent contained neither spermatids nor sperm (top of

Fig. 23). This focal absence of spermiogenesis was not seen in the controls. In the lumina of those tubules without spermiogenesis there were acidophilic debris and a few irregular pyknotic sperm. This debris was seen occasionally in smaller amounts in a few of the tubules containing normal numbers of maturing sperm.

Eighteen days after the 250  $\mu$ c. injection there was almost complete loss of the spermatogonia and primary spermatocytes. The secondary spermatocytes, which appeared normal except for occasional evidence of intra- and intercellular edema, were now adjacent to the basement membrane along with the apparently unaltered Sertoli cells. In addition, a slightly diminished number of intact spermatids remained (Fig. 23). Only a few of the remaining primary spermatocytes and a very few of the secondary spermatocytes were in mitosis. In 90 per cent of the tubules there were only spermatids and developing sperm with no remaining spermatocytes. In the lumina and among the seminiferous lining cells of many tubules there were spherical, amorphous, dark-staining masses about the size of a spermatocyte. Similar bodies were only occasionally seen in control testes. Presumably this series of animals presenting such a marked degree of

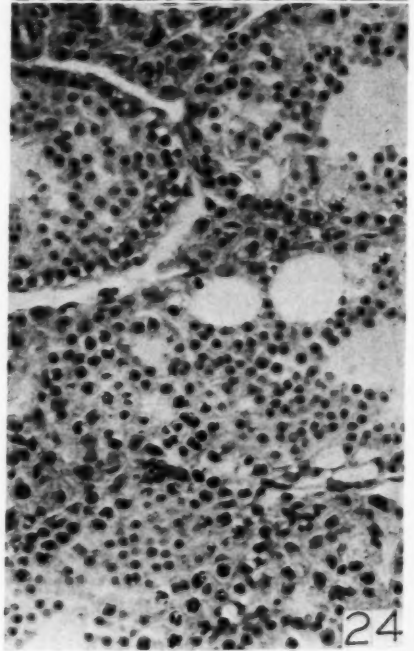
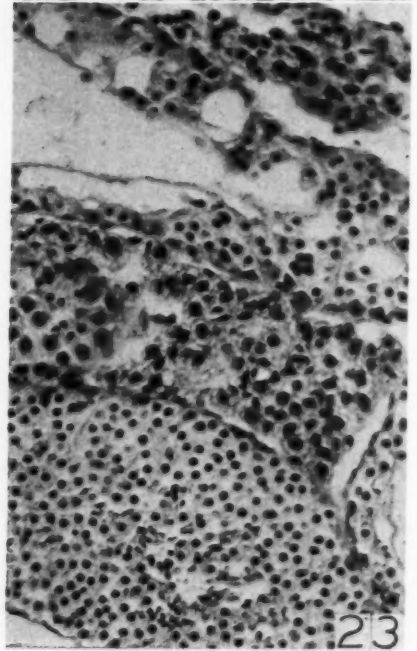
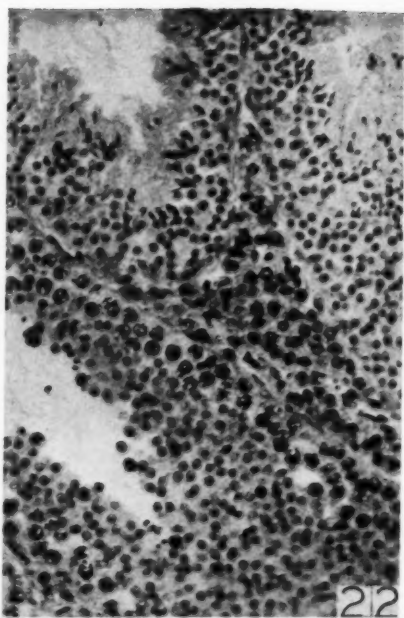
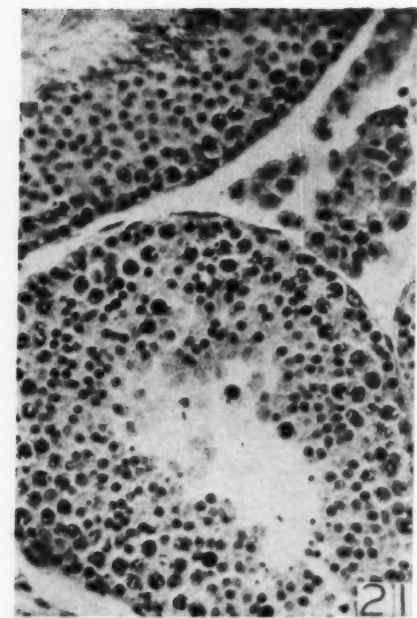


Fig. 21. Slight deterioration of the mature innermost sperm cells of seminiferous tubules and little other change in testes of mouse two days after injection of 250  $\mu$ c. of  $P^{32}$ .  $\times 250$ .

Fig. 22. Beginning increased numbers of interstitial cells nine days after injection of 250  $\mu$ c. of  $P^{32}$ , compared to two-day photomicrograph (Fig. 21).  $\times 250$ .

Fig. 23. Foamy, closely packed interstitial cells of mouse testis and totally degenerated seminiferous tubules (top) at eighteen days after injection of 250  $\mu$ c. of  $P^{32}$ .  $\times 250$ .

Fig. 24. Increased numbers of interstitial cells; vacuoles in tubular epithelium and no mature sperm cells, at fifty days after injection of 250  $\mu$ c. of  $P^{32}$ .  $\times 250$ .

injury after a dose of 250  $\mu$ c. is a temporarily sterilized group.

The most striking feature fifty days after injection was the absence of spermiogenesis and the return of the immature forms which were absent in those specimens seen at twenty days. There was much more variation in tubular structure in these specimens than in the controls (Fig. 24). The spermatogonia appeared in approximately normal numbers in most of the tubules and showed normal mitotic activity. In the few tubules where the number of spermatogonia was still decreased, there was an increase in the number of Sertoli cells, which except for occasional excessive vacuolization were not unusual. There was still a markedly reduced number of primary and secondary spermatocytes. Large intercellular vacuoles were seen among the seminiferous cells (Fig. 24). There was very little spermiogenesis, as evidenced by the paucity of spermatids, immature sperm, and adult sperm. The few remaining sperm were atypical and irregular.

*Interstitial cells* two days after injection showed a questionable increase in both size and vacuolization of cytoplasm, which progressed until nine days after injection, when there was also an increased number of interstitial cells (Fig. 22). By twenty days a definite increase in size and number of interstitial cells was noted. Distinct hyperplastic clumps of interstitial cells exhibiting occasional mitoses were found between most of the tubules. There also appeared to be a slight increase in cytoplasmic vacuolization (Fig. 24). At fifty days there was a maximum increase in the number of interstitial cells, all of which were markedly vacuolated and had a foamy acidophilic appearance (Fig. 24).

Immediately after injection of 2 mc. of  $P^{32}$ , the general tissue pattern remained undisturbed, although some cytologic changes were evident: a small amount of intercellular edema; decreased Sertoli cells; and in the lumina of the seminiferous tubules, abnormal spermatids. In addition, there were a few degenerated sperm cells appearing as amorphous basophilic

spheres in the tubules (compare damage in Fig. 33 with normal testis, Fig. 32).

*Discussion and Summary:* Radiation injures first the least mature of the spermatogenic cells, as evidenced by nearly complete loss of spermatogonia after nine days of irradiation with 250  $\mu$ c. of  $P^{32}$ . The primary spermatocytes were the next to show injury, disappearing after twenty days of exposure, when the process of spermiogenesis was also greatly retarded. The secondary spermatocytes and Sertoli cells were not appreciably altered.

The pattern of radiation injury might be explained by an early loss of spermatogonia and therefore a loss of source of spermatocytes. As the primary spermatocytes undergo mitotic division and form secondary spermatocytes, they are not replaced. Then, when secondary spermatocytes form spermatids, they are not replaced. Thus, after twenty days exposure, some of the tubules contained only spermatids, premature sperm, and Sertoli cells, with no immature spermatogenic forms. It is probable that irradiation injury does not affect all the cells of the seminiferous epithelium equally, and a very few spermatogonia survive the damage. The remaining spermatogonia began to regenerate sometime before or by fifty days after injection of 250  $\mu$ c. This accounts for the groups of immature forms seen at that time. No mature sperm or spermatids were found at fifty days.

The interstitial cells showed two changes: first, increased vacuolization, as seen in the nine-, twenty-, and fifty-day testes, and second, proliferation as seen in the twenty- and fifty-day testes. This finding is consistent with the hyperplasia often associated with tubular injury and degeneration seen in human material.

#### KIDNEYS

The kidneys of the animals injected with 25  $\mu$ c. of  $P^{32}$  showed no morphologic changes. At ten days in the kidneys of the animals injected with 250  $\mu$ c. there was occasional shrinking of the epithelial cells lining the renal tubules. This was a scattered, spotty effect, such as is seen in

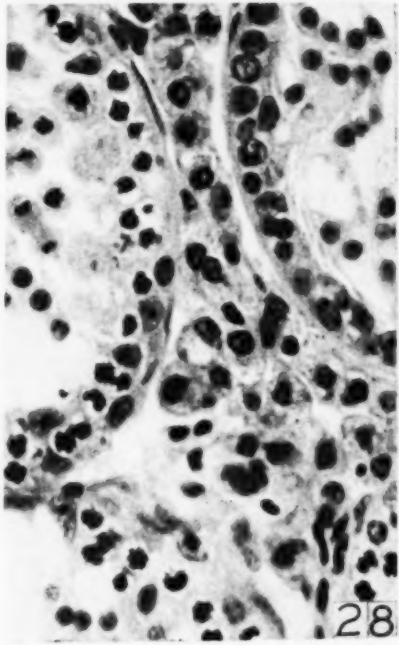
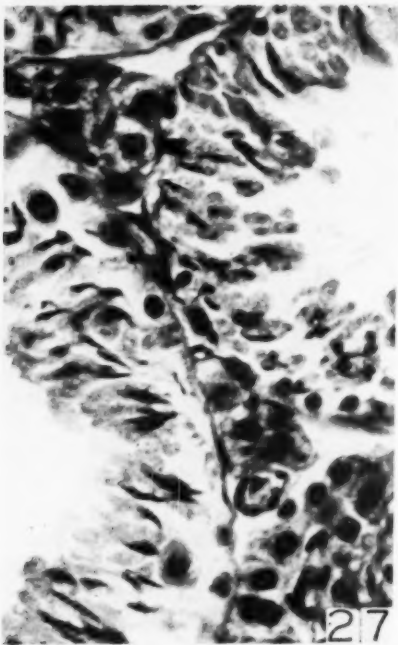
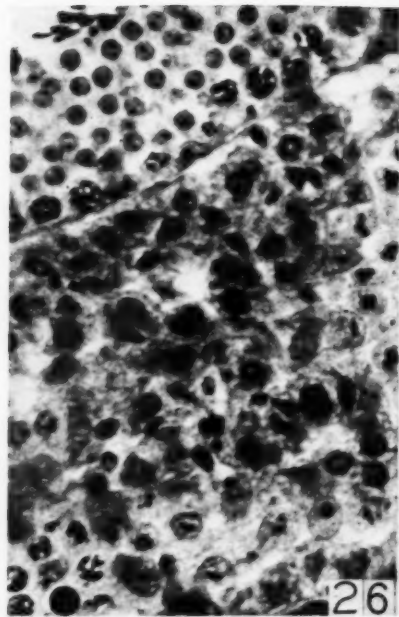
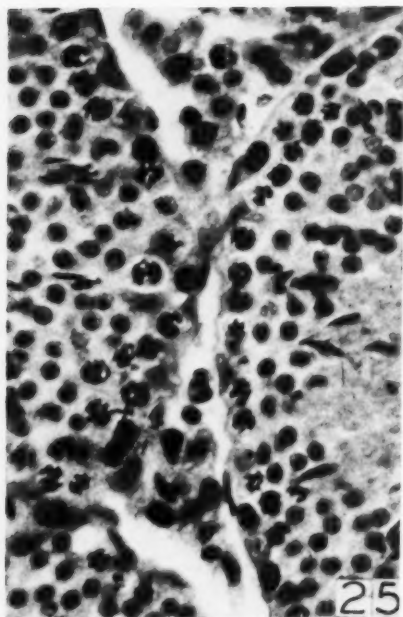


Fig. 25. Normal amount and structure of testicular interstitial cells and normal spermiogenesis.  $\times 500$ .

Fig. 26. Scanty numbers of spermatogonia along basement membrane (top) and foamy appearance of interstitial cells (lower), nine days after injection of 250  $\mu\text{c}$ . of  $\text{P}^{32}$ .  $\times 500$ .

Fig. 27. Loss of all primary spermatocytes and spermatogonia twenty days after injection of 250  $\mu\text{c}$ . of  $\text{P}^{32}$ .  $\times 500$ .

Fig. 28. Absence of primary and secondary spermatocytes and spermatids; only basal row spermatogonia remaining; prominent interstitial cells. Fifty days after injection of 250  $\mu\text{c}$ . of  $\text{P}^{32}$ .  $\times 500$ .

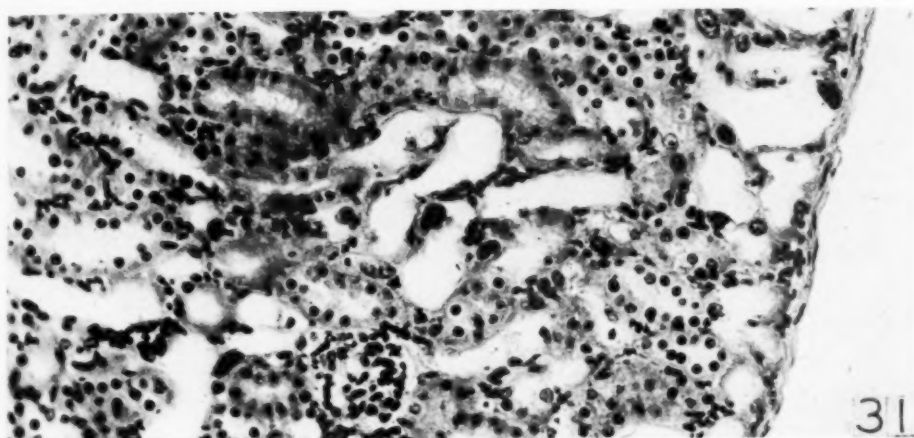
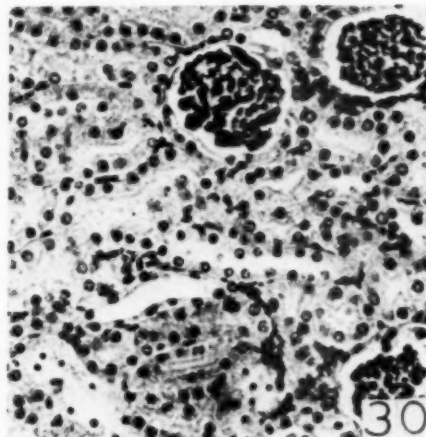
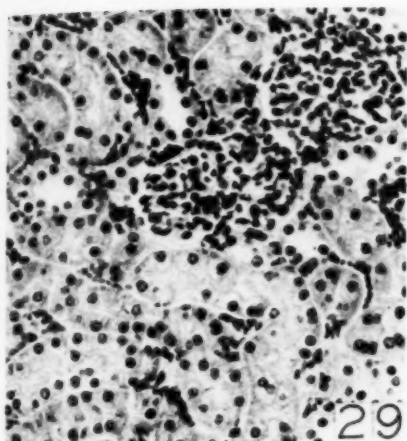


Fig. 29. Normal mouse kidney.  $\times 250$ .

Fig. 30. Kidney of mouse injected with 2 mc. of  $P^{32}$  (lethal dose) shows at five days little change except for pyknotic cells of proximal tubules.  $\times 250$ .

Fig. 31. Kidney of mouse injected with 250  $\mu$ c. of  $P^{32}$ , living eighteen days, shows marked tubular changes.  $\times 250$ .

Figure 31. No change could be seen in the glomeruli, and no inflammatory or vascular changes were found after this dosage. By the thirteenth to fifteenth day after injection the degenerative effect on the tubules seemed maximal, and there was beginning regeneration of the epithelial cells. This is seen in Figure 31, where large dividing cells are present along with the empty tubules desquamated of cell linings. At fifty days no change produced by irradiation could be seen in the kidneys.

A dose of 2 mc. caused death of the ani-

mals before the development of any renal changes other than those described and seen in Figure 30.

#### ADRENAL GLANDS

The adrenals showed no specific radiation effects but slight variable congestion was observed, which was not correlated with the amount of radiation received.

#### DIGESTIVE TRACT

With doses of 25  $\mu$ c. and 250  $\mu$ c. the esophagus and stomach of almost all of

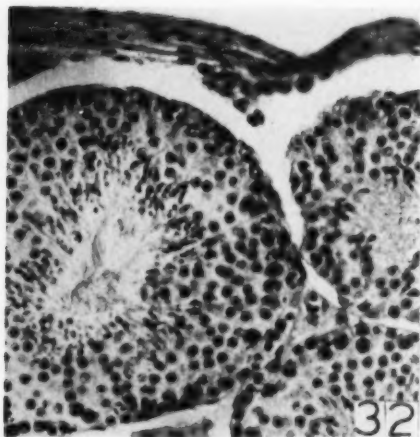


Fig. 32. Normal mouse testis.  $\times 250$ .

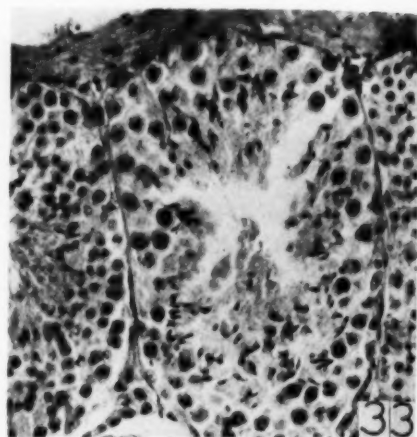


Fig. 33. Testis of mouse injected with lethal 2 mc. dose of  $P^{33}$ , showing spermatogenesis still existing at death (five days).  $\times 250$ .

the experimental animals were apparently unaffected morphologically. Two days after a dose of  $250 \mu\text{c.}$ , mitoses of the basal glandular epithelium of the ileum had stopped and superficial desquamation occurred (Fig. 36). Four days after injection, this latter effect was absent and the mucosa appeared less injured. No histologic changes were found which could be correlated with the severe diarrhea exhibited clinically by this group.

In the group receiving 2 mc. the terminal ileum and colon showed desquamation of the epithelium covering the ends of the villi and marked vacuolization of the remaining epithelium. The cells were swollen, the nucleoli were large, and intranuclear vacuoles were present. The submucosa was edematous and congested, with occasional red blood cells in the bowel lumen, but no gross hemorrhage originated from the bowel walls (Fig. 38).

#### SPINAL CORD

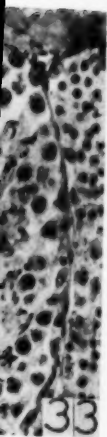
In a few instances, small petechial extravasations of blood were noted in the ventral horns of the spinal cord of the mice receiving  $250 \mu\text{c.}$  In addition, at least two large central hematomas extended vertically in the cord, over a distance of two vertebral segments.

#### LUNGS

Except for variable degrees of congestion, there were no specific radiation changes in the lungs of any of the animals. However, pneumonia was observed frequently and was associated probably with leukopenia and generalized debility resulting from the irradiation.

#### LIVER

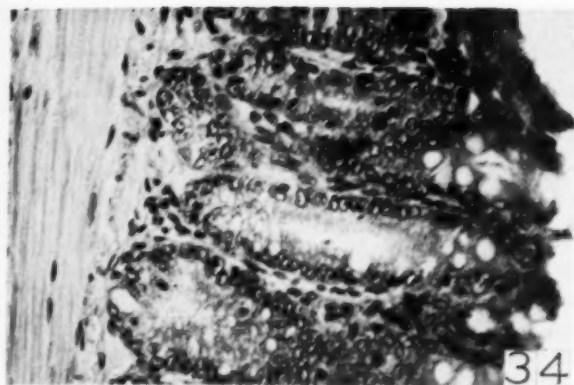
Very early in the course of irradiation no nuclear changes in the parenchymal cells could be seen, but the cytoplasm showed incomplete vacuolization and peculiar granular condensations. An outstanding feature of the liver seen at fifteen to twenty days was the compensatory ectopic hematopoiesis, present as multiple small foci of 6 to 15 cells (Fig. 37). The cells of these foci were largely of the granulocytic series at twenty days, but at fifty days there could be seen focal multiplication of cells of the erythrocytic series also. The maximum radiation effect on the liver, found about twenty to fifty days after injection, was a tendency toward regeneration of liver tissue shown by numerous mitotic figures in the liver cells (Fig. 37). Small amounts of pigment remained in fixed macrophages, and an occasional focus of fibrosis infiltrated with polymorphonuclear



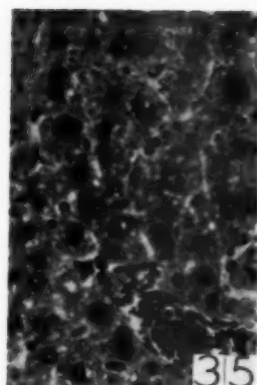
still existing at

s of conges-  
e radiation  
the animals.  
observed fre-  
probably with  
bility result-

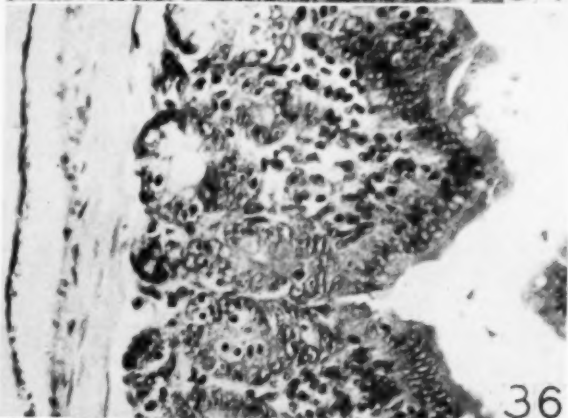
radiation no  
thymal cells  
ism showed  
ecular gran-  
standing fea-  
to twenty  
pic hemato-  
small foci of  
cells of these  
cytic series  
days there  
ion of cells  
The maxi-  
ver, found  
after injec-  
eneration  
ous mitotic  
7). Small  
d in fixed  
al focus of  
phonuclear



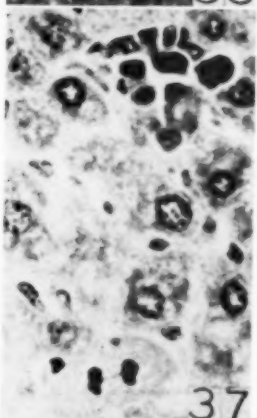
34



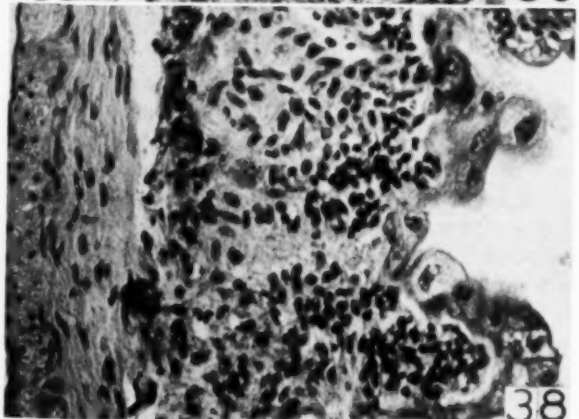
35



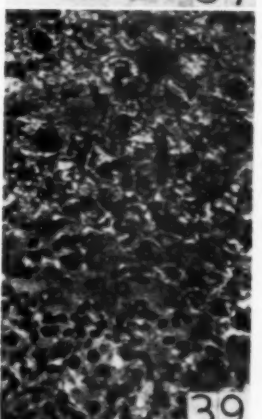
36



37



38



39

- Fig. 34. Normal mucosa of lower ileum.  $\times 300$ .  
Fig. 35. Normal mouse liver.  $\times 300$ .  
Fig. 36. Ileum of mouse two days after injection of 250  $\mu\text{c.}$  of  $\text{P}^{32}$ .  $\times 300$ .  
Fig. 37. Liver of mouse twenty days after injection of 250  $\mu\text{c.}$  of  $\text{P}^{32}$ . Note mitotic figures, myelocytes, foci of myeloid metaplasia, pyknotic parenchymal cells with granularity of cytoplasm.  $\times 300$ .  
Fig. 38. Ileum of mouse five days after injection of 2 mc. of  $\text{P}^{32}$ . Note hydropic change in epithelium, hemorrhage and edema of submucosa. Compare with Figs. 34 and 36.  $\times 300$ .  
Fig. 39. Liver ninety days after injection of 250  $\mu\text{c.}$  of  $\text{P}^{32}$ . Compare with Fig. 37, which is regenerating twenty days after injection. Note foci of fibrosis with inflammation at inferior margin.  $\times 300$ .

cells was also present (Fig. 39). An earlier stage of this focal fibrosis was seen sixteen days after injection as a pale-staining area of localized necrosis. At this time there was extreme variability of the size of the nuclei of the parenchymal cells of the liver.

#### SUMMARY

This is Part II of a detailed histologic examination of 82 mice injected with varying dosages of  $P^{32}$ , observed over periods of five to eighty-four days. The changes seen in the ovaries, testes, kidneys, adrenal glands, digestive tract, spinal cord, lungs, and liver are described.

25 Shattuck Ave.  
Boston 15, Mass.

#### REFERENCES

1. ALLEN, E.: Ovogenesis During Sexual Maturity. *Am. J. Anat.* **31**: 439-481, May 1923.
2. DE RÉNYI, G. S., DE RÉNYI, M., AND MURPHY, D. P.: Preconception Ovarian Radium Irradiation of Albino Rat. *Am. J. Roentgenol.* **28**: 764-783, December 1932.
3. GENTHER, I. T.: Irradiation of the Ovaries of Guinea Pigs and Its Effect on the Oestrous Cycle. *Am. J. Anat.* **48**: 99-137, May 1931.
4. MAXIMOW, A. A., AND BLOOM, W.: A Textbook of Histology. Philadelphia, W. B. Saunders Company, 1939, p. 540.
5. PINCUS, G.: The Eggs of Mammals. *Exp. Biol. Monographs*. New York, The Macmillan Co., 1936.
6. SCHMIDT, I. G.: Changes in the Genital Tracts of Guinea Pigs Associated with Cystic and "Interstitial Gland" Ovaries of Long Duration. *Endocrinology* **24**: 69-81, January 1939.
7. WARREN, S., MACMILLAN, J. C., AND DIXON, F. J.: Effects of Internal Irradiation of Mice with  $P^{32}$ . Part I: Spleen, Lymph Nodes, Thymus, Bone and Bone Marrow. *Radiology* **55**: 375-389, September 1950.

#### SUMARIO

#### Efectos de la Irradiación Interna de los Ratones con $P^{32}$ : Gonados, Riñones, Suprarrenales, Tracto Digestivo, Médula Espinal, Pulmones e Hígado

Esta es la Parte II de un pormenorizado examen histológico de 82 ratones inyectados con varias dosis de  $P^{32}$  (2,000  $\mu\text{c.}$ , 250  $\mu\text{c.}$  y 25  $\mu\text{c.}$ ; véase además la Parte I, en *Radiology* **55**: 375, septiembre, 1950). Discútense ahora los efectos sobre los ovarios, testículos, riñones, suprarrenales, tubo digestivo, médula raquídea, pulmones e hígado.

El efecto más teatral en los ovarios consistió en la disminución en tamaño, debida a: (1) menor número de folículos de Graaf, (2) ausencia de cuerpos amarillos y (3) condensación del estroma. Este último factor, unido al tardío desarrollo de tejido intersticial, está considerado como el más distintivo efecto postirradiatorio del  $P^{32}$  sobre el ovario.

El primer efecto en los testículos consistió en lesión de los espermatogonos menos maduros, expresada en forma de pérdida casi total de la espermatogonia al cabo de nueve días de irradiación con 250  $\mu\text{c.}$  de  $P^{32}$ . Los espermatocitos primarios fueron los que mostraron después lesión, desapareciendo tras veinte días de exposi-

ción, para cuya fecha la espermatogonia también estaba considerablemente retardada. Las células intersticiales revelaron aumento de la vacuolización y la proliferación.

Las alteraciones evocadas en los riñones y suprarrenales fueron leves y pasajeras.

Con las dos dosis más pequeñas los efectos en el tubo digestivo no fueron de mayor importancia. Con la dosis mayor (2 mc.) ocurrieron alteraciones hidrópicas en el epitelio y edema y congestión de la submucosa de la porción terminal del ileon y del colon, pero sin hemorragia macroscópica de la pared intestinal.

La médula espinal reveló pequeñas extravasaciones petequiales en algunos casos y grandes hematomas centrales en dos.

En los pulmones no se observaron alteraciones específicas debidas a la irradiación.

El efecto máximo en el hígado, descubierto de veinte a cincuenta días después de la inyección de  $P^{32}$ , fué una tendencia a la regeneración de tejido, revelada por numerosas figuras carioquinéticas en las células hepáticas.

## Deposition of Radiogallium ( $Ga^{72}$ ) in Proliferating Tissues<sup>1</sup>

H. C. DUDLEY, Ph.D., G. W. IMIRIE, JR., B.S., and J. T. ISTOCK

IT HAS PREVIOUSLY been shown, chemically and autoradiographically, that gallium enters bone at a rapid rate, following injection of the citrate or lactate, concentrating in those areas considered to have marked osteogenic activity (1, 2, 3).

The purpose of the present investigation was to study in experimental animals the deposition of radiogallium ( $Ga^{72}$ ) in proliferating tissues. The work comprised three parts: (a) the quantitative determination of the amount of  $Ga^{72}$  deposited in normal and growing bone and in healing fractures, (b) a pilot study of the degree of deposition of gallium in certain neoplastic conditions, (c) development of technics to provide greater detail in the autoradiographs of tissue containing  $Ga^{72}$ .

The isotopes of gallium which appear to have greatest promise for biological studies are  $Ga^{72}$  (14.3 hours half-life, 2.5 mev  $\gamma$ , 3.1 mev  $\beta^-$ ) and  $Ga^{67}$  (78.3 hours half-life, K capture, 0.3 mev  $\gamma$  with conversion  $e^-$ ). The  $Ga^{72}$  can be prepared by neutron bombardment of magnetically separated  $Ga^{71}$  to produce an initial specific activity of about 1.0 mc.  $Ga^{72}$ /mg. Ga. By deuteron bombardment ( $d, n$ ) of a zinc target in a cyclotron, the isotope  $Ga^{67}$  can be produced, accompanied by a quantity of  $Zn^{65}$  (250-day half-life). This and other contaminants may be eliminated by ether extraction of gallium from a 6 N HCl solution.

The studies described herein were carried out with  $Ga^{72}$  supplied by the Atomic Energy Commission. The natural element ( $Ga^{69} + Ga^{71}$ ) was activated by the ( $n, \gamma$ ) reaction, and an initial activity of about 0.4 mc./mg. Ga was obtained. On administration to animals, the activity was

reduced by decay to about 0.2 mc./mg. Ga.

### METHODS

*Preparation of gallium ( $Ga^{72}$ ) citrate:* Quartz ampules were prepared and sufficient purified gallium nitrate was added to provide 75 mg. gallium (5). These ampules were flame-sealed and irradiated in the pile by the Atomic Energy Commission. The initial activity was approximately 30 millicuries (mc.); when shipped by air, the gallium could be administered with an activity of 12-15 mc.

*Preparation of the gallium for injection* was as follows:

- (a) Add to the opened ampule 1 c.c. hot HCl (1:1). Heat gently to facilitate solution of the solid. Pour into a graduate cylinder, and rinse ampule with 2-c.c. portions of water.
- (b) Add 1 c.c. of brom-cresol purple indicator.
- (c) Add 2 c.c. of 20 per cent citric acid solution. Mix.
- (d) Add concentrated NaOH solution to a pH of 6-7. Color should be red-purple.
- (e) Make to required volume with water. In our work, 20 c.c. was convenient, since this gave an activity of about 1 mc./c.c.

Observe precautions and provide adequate shielding (5, 6).

The solution prepared as described is suitable for subcutaneous injection if the area is anesthetized, *i.e.*, with procaine.

*Intravenous administration* may produce acute reactions, often fatal, due to the effect of the citrate on blood calcium. This effect has been overcome by the simultaneous administration of 0.5 gm. calcium chloride for each 10 c.c. of the  $Ga^{72}$  citrate solution. The most convenient method of intravenous administration is by means of glucose-saline infusion with the gallium

<sup>1</sup> From the Naval Medical Research Institute, National Naval Medical Center, Bethesda, Md. The opinions or conclusions contained in this report are those of the authors. They are not to be construed as necessarily reflecting the views or endorsement of the Navy Department.

Presented in part at the Thirty-fifth Annual Meeting of the Radiological Society of North America, Cleveland, Ohio, Dec. 4-9, 1949.

and calcium being introduced into the rubber tube just above the hypodermic needle. The rate of infusion should be moderate, and sufficient of the infusion fluid should be allowed to dilute the gallium so that no localized reaction occurs.

**Radiometric Assay:** In the determination of  $Ga^{72}$  as reported in these studies, the quantitative estimations were carried out on whole fresh tissues, without drying, by making gamma counts at constant geometry. The end-window Geiger tubes were shielded with an aluminum absorber of 1,700 mg./cm.<sup>2</sup>, which absorbed all beta radiation and back-scatter. By this method, differences due to tissue density and self absorption were eliminated. Because of the high counting rates of samples and the consistently high counting yield, this assay gives results with an error of less than  $\pm 10$  per cent.

In the quantitative determination of  $Ga^{72}$  (expressed as mc. of  $Ga^{72}$ ), samples of the initial citrate solution were compared with standard quantities of radium (1 to 2 mg. in 0.5 mm. Pt needles) by means of an ionization chamber meter or a quartz fiber electroscope. The samples were mounted a constant distance from the center of the chamber of the meter or the electroscope, with the  $Ga^{72}$  being shielded by means of a 2-mm. brass shield. By this means, the beta radiation was absorbed and the gamma emission of the  $Ga^{72}$  was compared with gamma emission of a standard radium source.

**Sample Calculations:**

- 1 millicurie (mc.). Amount of radon in equilibrium with 1 mg. of radium.
- 1 mg. Ra yields at 1 meter 0.84 mr./hr. (millicurie/hour).
- 1 mc.  $Ga^{72}$  yields at 1 meter 1.32 mr./hr. (calculated from data of Haynes (9)).

**Ionization chamber meter (Victoreen 247A)**

1.969 mg. Ra at 1 meter. = 1.65 meter reading  
7.5 mg. Ga (in 5 c.c.) at 1 meter = 1.98 meter reading

$$\frac{Ga^{72} \text{ reading} \times \text{mg. Ra} \times 0.84}{\text{Ra reading} \times 1.32} = \text{millicuries } Ga^{72}$$

$$\frac{1.98 \times 1.969 \times 0.84}{1.65 \times 1.32} = 1.50 \text{ mc. } Ga^{72}$$

**Electroscope (Lauritsen)**

1.969 mg. Ra at 50 cm. = 50 division in 2.55 min.  
7.5 mg. Ga at 50 cm. = 50 division in 2.14 min.

$$\frac{\text{mg. Ra} \times \text{time of Ra} \times 0.84}{\text{Time of Ga} \times 1.32} = \text{millicuries } Ga^{72}$$

$$\frac{1.969 \times 2.55 \times 0.84}{2.14 \times 1.32} = 1.49 \text{ mc. } Ga^{72}$$

**EXPERIMENTAL**

**Concentration of  $Ga^{72}$  in Bone:** Young rabbits (2.0–2.5 kg.) were anesthetized and one foreleg was broken. The leg was then placed in a cast and the animals were housed in cages for seven to twenty-one days. At intervals (seven, fourteen, twenty-one days) following the fracture, rabbits were injected subcutaneously with radiogallium ( $Ga^{72}$ ) citrate (0.5 mc./kg.) and sacrificed sixteen hours after the injection. Samples of both normal bone and the healing callus were examined autoradiographically (3), and the concentrations of gallium in various portions of the fresh bone were determined by photographic densitometric measurements (4), and by means of radiochemical gamma-counting techniques.

Immediately after completion of the autoradiographs, the bones were cut into various fractions by means of a thin abrasive wheel. In this way those areas of greatest osteogenic activity (callus, epiphysis) were obtained relatively free of extraneous tissue and adjacent cortical or trabecular bone. The weighed fresh samples were gamma-counted and compared with standard solutions containing  $Ga^{72}$ . Results of these findings are summarized in Table I and Figure 1, A and B. Results indicate that in the young rabbit the epiphyseal junction absorbs four to five times the concentration of gallium deposited in the adjacent bone. The callus of the healing fracture concentrates gallium to a degree two to three times that found in the bone adjacent to the fracture.

These findings indicate that gallium enters into the processes of normal bone growth and repair, with particular affinity for those areas where osteogenic activity is greatest. No significant differences

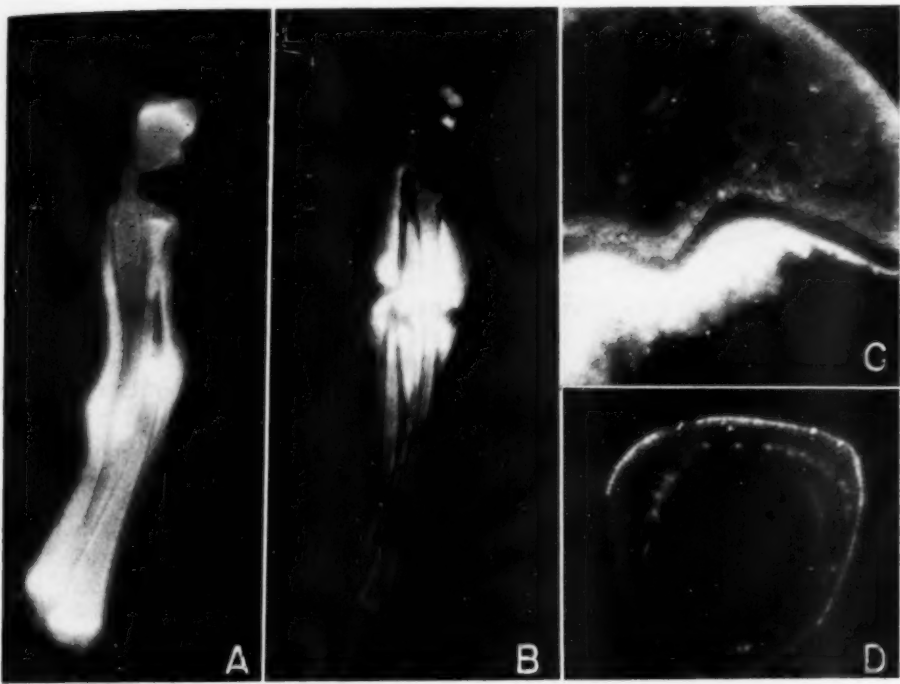


Fig. 1. Prints of autoradiographs of rabbits receiving 0.5 mc. Ga<sup>72</sup>/kg. A and B. Healing fractures of foreleg fourteen days after break, showing deposition of Ga<sup>72</sup> in callus. X1. C. Head of femur, showing area at epiphyseal junction. X7. D. Cross section of shaft of femur showing localization of Ga<sup>72</sup>. X7.

TABLE I: CONCENTRATION OF GALLIUM (Ga<sup>72</sup>) IN GROWING AND HEALING BONE OF RABBITS

—Microcuries per Gram of Fresh Bone—		
Sample	Determined Autoradiographically	Determined by Gamma Counting
Normal Bone		
Epiphyseal junction	4.0	3.9
Trabecular	1.1	1.6
Cortical	0.8	0.9
Healing Bone		
Callus (14 days)	3.1	2.2

Note: Values here are the mean of samples from four animals. Reference standards of Ga<sup>72</sup> were prepared and used to estimate the concentrations at time of death.

were noted in the deposition of Ga<sup>72</sup> in the fourteen to twenty-one days following the fracture. At seven days there was a diffuse, less well defined deposition in the areas surrounding the fracture.

**Deposition of Ga<sup>72</sup> in Neoplastic Tissues:** In order to determine the affinity of gallium for various neoplastic growths, a group of animals having spontaneous non-

osteogenic neoplasms were injected subcutaneously with 0.5 mc. Ga<sup>72</sup>/kg., as the citrate, and sacrificed fourteen to sixteen hours thereafter. The tissues were removed and gamma counts made by the methods previously described.

In Table II is given a résumé of the results of these studies with one strain of rat, one strain of mouse, and one dog. It will be seen that no significant localization of Ga<sup>72</sup> occurred in the fibroadenoma or the fibrocarcinoma of the rat and mouse or in the mixed mammary tumor of a dog. While localization in the tumor was always greater than that seen in the muscle of the corresponding animal, this deposition did not approach the concentrations found in the osteoid structures.

In order to determine the degree of localization of Ga<sup>72</sup> in osteogenic lesions, a transplanted osteogenic sarcoma of the mouse was introduced subcutaneously on the abdominal wall of several mice (C<sub>3</sub>H

TABLE II: COMPARATIVE CONCENTRATIONS OF  $Ga^{72}$  IN NORMAL AND NEOPLASTIC TISSUES

Species	No. of Animals	Gamma Counts per Minute per Gram of Fresh Tissue						Type Tumor
		Composite Bone	Kidney	Liver	Spleen	Muscle	Tumor	
Albany rat	4	7,990	6,081	1,115	693	140	313	Fibroadenoma
Mouse ( $C_3H$ )	2	620	373	136	106	59	219	Fibrosarcoma
Dog	1	2,273	2,853	325	111	17	245	Mixed mammary tumor

Note: The results shown above are the mean of at least duplicate samples taken from the indicated number of animals. Counts are corrected for background and are calculated to time of death.

strain). One of these mice was injected subcutaneously with 0.5 mc.  $Ga^{72}$ /kg. as the citrate, and the tumor was removed after sixteen hours. An autoradiograph was prepared of the dense tumor tissue, which indicated localization of  $Ga^{72}$  in this mass equivalent to that found in the epiphyseal junction or healing fractures of rabbits, namely 3-5  $\mu$ c./gm. (microcuries/gram) of tissue (Fig. 2).

Additional serial transplants of this tumor produced a fibrous mass different in character from the original tumor. When autoradiographs of these soft masses were prepared, it was found that in only a few small discrete areas was there any localization of  $Ga^{72}$ . This indicates that, while the mass of the tumor was fibrous in nature, there were centers of osteogenic activity still present.

It is recognized that the number of animals having spontaneous tumors presented in this report is small. However, the difficulties of obtaining spontaneous tumors in experimental animals on a laboratory basis has not permitted further extension of these studies. The data presented must be considered as a pilot study. The results are given in order to provide the best available basis for further investigation.

**Autoradiographic Technics:** The degree of definition obtainable by autoradiographic technics applied to  $Ga^{72}$  is determined by the penetration of the beta spectrum of this radioactive isotope. Since the maximum beta energy is 3.1 mev, there appears in the autoradiograph a somewhat indistinct outline caused by the scattering of the high-energy particles, not only by the tissue specimen but also by the emulsion,

the film, and the slide backing. The sharpness of the image is also reduced due to *Bremstrahlung* produced by the accompanying gamma spectrum (max. 2.5 mev).

Technics have been improved over those previously reported (3) and include a method which permits the production of a more detailed survey type autoradiograph from undecalcified bone specimens using the short half-life 14.3-hr. isotope,  $Ga^{72}$ . The animals were injected subcutaneously with 1 mc.  $Ga^{72}$ /kg. as the citrate and killed four hours after injection, which permitted about 75 per cent of the maximum absorption of  $Ga^{72}$  to take place in the bone. The animal was then sacrificed and the bone specimens were removed and immediately sectioned to a thickness of 0.10-0.12 mm. by means of a self-feeding circular saw (7). These sections were mounted on microscope slides with a minimum amount of warm (40° C.) photographer's gelatin. As the gelatin hardened, the slides were immersed in 90 per cent and then absolute ethanol for fixation and dehydration. Fixing time did not exceed fifteen minutes. After drying, the bone specimens were placed in direct contact with the emulsion of panchromatic fine grain film (Weston speed, daylight, 50). The film and specimens were held in close contact by mounting between two aluminum plates, on each of which were pasted two layers of blotting paper, covered with black paper. The whole was held tightly together by means of two screw clamps (C type). The specimens were left in contact with the film for sixteen hours, after which the film was slightly overdeveloped in ultra-fine grain developer (Von-L No S-35; 7 minutes at 20° C.) to bring out

greater detail with minimum grain size. In Figure 1, C and D, are shown enlarged ( $\times 7$ ) prints of the autoradiograph of sections of the head and shaft of the femur of a young rabbit (1.5 kg.).

A modification of a technic previously described (8) has proved useful in producing autoradiographs having good definition. A special emulsion (Ansco, autoradio-

scope slides. The unstained silver-impregnated sections are used for photographic reproduction, but microscopic examination is best done after staining lightly with hematoxylin-eosin. The autoradiographs in Figure 3 ( $\times 100$ ) were made as described, from a bone taken from a mature rabbit four hours after intravenous injection of 1 mc.  $\text{Ga}^{72}$ /kg., as the citrate.

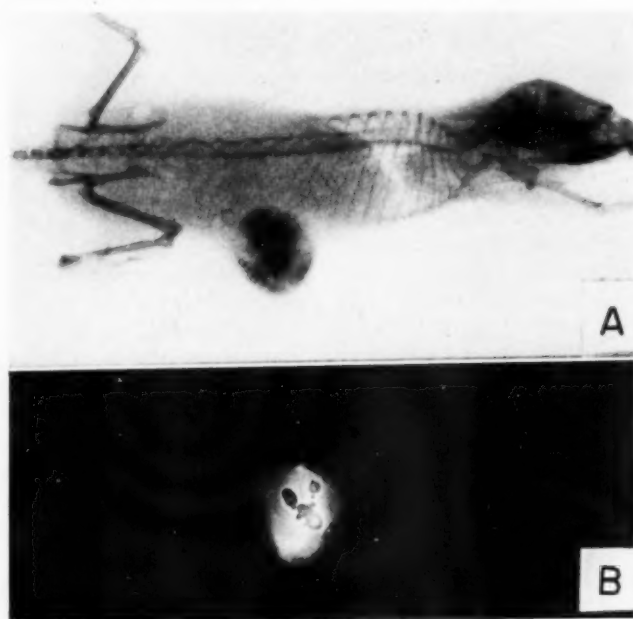


Fig. 2. A. Roentgenogram showing transplanted osteogenic sarcoma in mouse.  $\times 1$ . B. Autoradiograph of tumor sixteen hours after subcutaneous injection of 0.5 mc. of  $\text{Ga}^{72}$ /kg.  $\times 1$ .

graphic "A") was obtained in the fresh semisolid state, melted at  $40^\circ \text{C}$ ., and diluted with two volumes of water plus a few drops of a wetting agent. This diluted emulsion was used to impregnate fresh undecalcified bone sections (0.1 mm.) cut as described above. The impregnated sections were dried at  $38^\circ \text{C}$ . for thirty minutes, and were then placed in a light-tight container for sixteen to twenty-four hours. They were then slightly overdeveloped in the fine grain developer. After fixing in 30 per cent hypo followed by acid hardener, the sections were cleared in xylol and mounted in balsam on micro-

These autoradiographic studies extend earlier ones (3). The findings indicate that  $\text{Ga}^{72}$  is deposited in the periosteum, the endosteum, in the lining of the blood vessels, in the haversian canals, and in the calcifying cartilage at the ends of the diaphysis. The trabeculae of cancellous bone are outlined by the  $\text{Ga}^{72}$ , since it is presumed to be laid down in the endosteum. The epiphyseal cartilage plate appears to contain little or no  $\text{Ga}^{72}$ , while the fine structure of the adjacent epiphysis is clearly outlined. The apparent deposition of  $\text{Ga}^{72}$  throughout cortical bone, as suggested by our earlier work, now appears

to be due to the deposition of  $Ga^{72}$  on the periphery of blood vessels and in the haversian canal system. The scattering of the energetic beta radiation by the dense bone gives an appearance in the gross autoradiographs (3) of a more or less homogeneous distribution of  $Ga^{72}$  in the shafts of the long bones.

The difficulties encountered with the autoradiographic study of  $Ga^{72}$ , particularly on the cellular level, are those due to its short half-life (14.3 hr.). The bone sections must be cut while fresh and placed in contact with some photographic emulsion within a few hours after the death of the animal. Since 70 per cent of the activity of the  $Ga^{72}$  deposited in the bones decays in twenty-four hours, it can be seen that the usual histologic methods of imbedding and cutting are not applicable. Other difficulties were encountered in using many types of photographic emulsions, since most are relatively insensitive to the gamma rays and beta particles given off by  $Ga^{72}$ . Also, in enlarging the contact autoradiographs, the size of the developed silver granules makes extensive magnification impractical. These difficulties have in part been overcome by the use of the slower fine grain panchromatic films and slight over-development in an ultra-fine grain developer. In cases of low intensity radiations, the use of special developers (Von-L, No. S-35) or intensifiers ("Hydram") added to the usual fine grain developers, has made possible the bringing out of the latent image more strongly. In general, the slower panchromatic emulsions rather than x-ray emulsions have given more satisfactory results when finer detail was desired.

#### DISCUSSION

Deposition of  $Ga^{72}$  in bone appears in many respects similar to that of other bone seekers (Ra, Pu,  $P^{32}$ ,  $Sr^{90}$ ). However, gallium is deposited more rapidly than many others and the short half-life does not offer such chance for the production of neoplastic growths. Localization of  $Ga^{72}$  in the endothelial cells of the skeletal

structures, and particularly the deposition of gallium in that zone of osteogenesis between the cartilaginous epiphyseal plate and the metaphysis (*i.e.*, the zone of calcifying cartilage), indicates that gallium enters into the calcification process in a dynamic manner. It is these tissues which are active in the development of new bone and the regeneration of changes of the haversian canal system, and it is in these areas that the phosphatases are believed to be most actively concentrated. Therefore, as a working hypothesis, it is suggested that the injection of small amounts of  $Ga^{72}$  citrate, followed by preparation of autoradiographs by the emulsion impregnation technic as described above, may provide a means of differential staining and localization of structures containing large amounts of the phosphatase enzymes.

The localization of gallium in osteogenic centers makes possible a more or less localized irradiation of these sites by means of  $Ga^{72}$ . This suggests that radiogallium may be useful in the therapy of osteogenic neoplasms. Also because of this localization, the *in situ* irradiation of osteoid structure may be useful in certain conditions in which whole body roentgen irradiation is now an accepted practice. By reason of its short half-life (14.3 hr.), repeated injections of this isotope would seem to offer a means of applying ionizing radiation of high intensity, in divided doses, with no danger of the residual radiation inherent in the use of the longer-life bone seekers.

In considering the therapeutic trial of  $Ga^{72}$ , the possible toxicity of the carrier gallium must be anticipated. In moderate doses this element produces nephritis followed by albuminuria and glycosuria. With an increase of specific activity of  $Ga^{72}$ , through the magnetic separation of  $Ga^{71}$ , resulting in a reduction of the carrier Ga, it is believed that experimental clinical trials will be warranted. This is in addition to the clinical studies of osteoid lesions and metastases with tracer (500  $\mu$ c.) quantities of  $Ga^{72}$  now being carried out.

the dep-  
of osteo-  
epiphys-  
i.e., the  
ates that  
n process  
se tissues  
nt of new  
anges of  
it is in  
ases are  
entrated.  
esis, it is  
of small  
owed by  
by the  
described  
fferential  
tructures  
phospha-

steogenic  
or less  
by means  
iogallium  
steogenic  
localiza-  
oid struc-  
onditions  
radiation  
y reason  
repeated  
seem to  
radiation  
, with no  
inherent  
ekers.

e trial of  
e carrier  
moderate  
nephritis  
ycosuria.  
tivity of  
ration of  
e carrier  
al clinical  
in addi-  
osteoid  
cer (500  
g carried

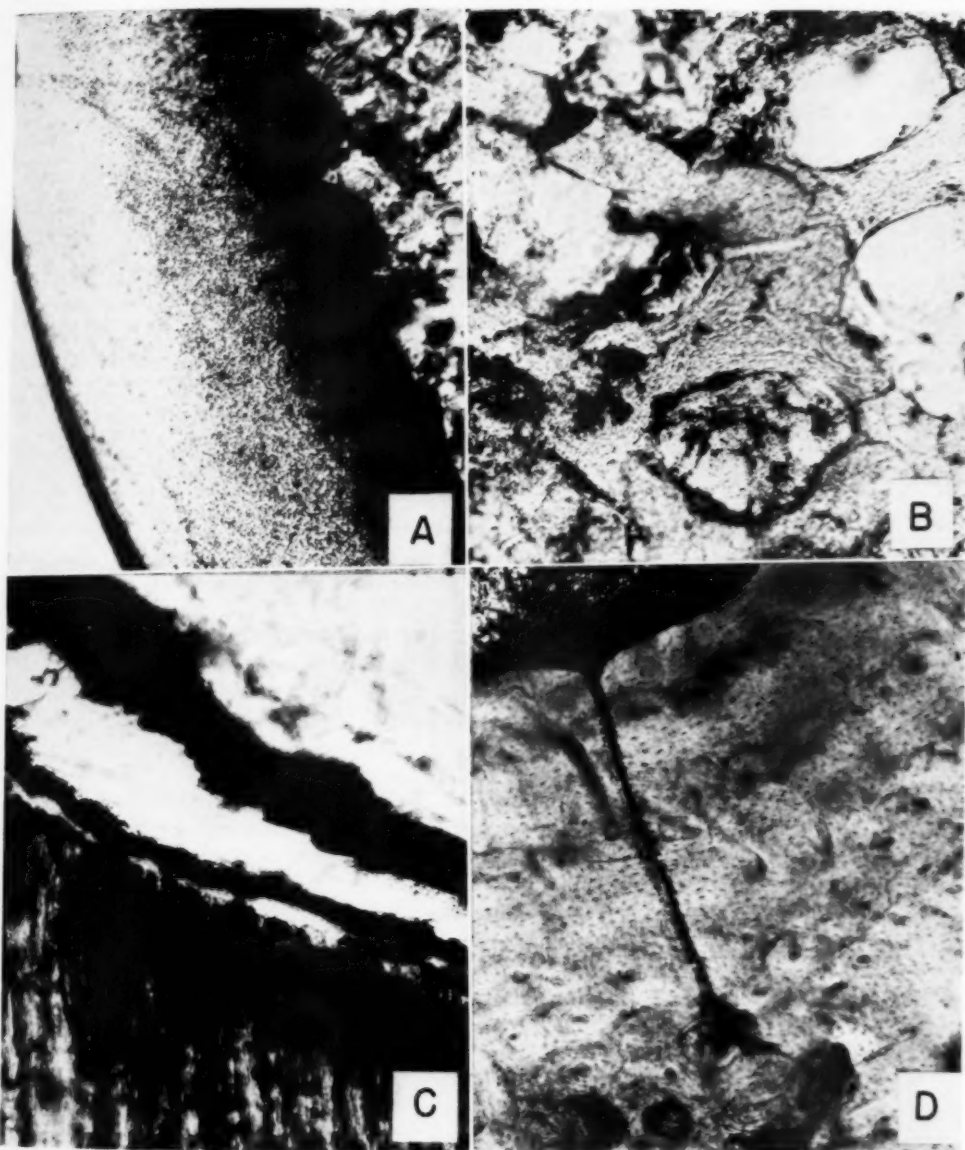


Fig. 3. Photographs ( $\times 100$ ) of 0.1-mm. bone sections of femur from 3.5-kg. rabbit, four hours after injection of 4 mc. of radiogallium ( $Ga^{72}$ ) citrate. Dense black areas are silver granules deposited from a photographic emulsion, affected by the radioactivity, and developed in the usual way:

- A. Head of condyle, showing outer layer of high  $Ga^{72}$  content, with underlying zone of cartilaginous material, followed by a zone of high  $Ga^{72}$  content, and finally by the trabeculae of the epiphysis.
- B. Details of  $Ga^{72}$  in the trabeculae of the epiphysis.
- C. Epiphyseal junction. Lower columnar area shows high content of  $Ga^{72}$ , increasing as the cartilaginous plate is approached. The white area in this plate is devoid of  $Ga^{72}$ , while above is an area of the epiphysis which is very rich in  $Ga^{72}$ .
- D. Nutrient vessel connecting the periosteal layer with an haversian canal. Note dense localization adjacent to periosteum.

## SUMMARY AND CONCLUSIONS

Radiogallium ( $Ga^{72}$ ) has been shown to concentrate at areas of osteogenic activity, *i.e.*, the epiphyseal junction and in the callus of healing fractures in rabbits, and in osteogenic sarcoma of the mouse.

In certain fibroadenomas, fibrosarcomas, and mixed mammary tumor of animals, no significant localization of  $Ga^{72}$  occurred.

Autoradiographic studies of the deposition of  $Ga^{72}$  in bone, by impregnation of bone sections with liquid photographic emulsion, has made possible more detailed localization of this element.

It is suggested that radiogallium citrate ( $Ga^{72}$ ) is worthy of clinical trials in tracer amounts for diagnostic purposes and at higher levels for possible therapeutic effect.

**ACKNOWLEDGMENTS:** The authors wish to acknowledge gratefully the assistance rendered by Professor E. J. Frick, Kansas State College, Manhattan, and Professor J. M. Wolfe, Albany (N. Y.) Medical College, for their assistance in obtaining tumor-bearing animals. Dr. W. H. Eyestone, National Cancer Institute, Bethesda, Md., kindly

supplied the mice having osteogenic sarcoma, and identified microscopically the classes of tumors mentioned in these studies.

## REFERENCES

1. DUDLEY, H. C.: Determination of Gallium in Biological Materials. *J. Pharmacol. & Exper. Therap.* **95**: 482-486, April 1949.
  2. DUDLEY, H. C., MADDOX, G. E., AND LARUE, H. C.: Studies of the Metabolism of Gallium. *J. Pharmacol. & Exper. Therap.* **96**: 135-138, June 1949.
  3. DUDLEY, H. C., AND MADDOX, G. E.: Deposition of Radiogallium ( $Ga^{72}$ ) in Skeletal Tissues. *J. Pharmacol. & Exper. Therap.* **96**: 224-227, July 1949.
  4. DUDLEY, R. A., AND DOBYNS, B. M.: The Use of Autoradiographs in the Quantitative Determination of Radiation Dosages from  $Ca^{45}$  in Bone. *Science* **109**: 327-328, April 1, 1949.
  5. DUDLEY, H. C.: Preparation and Properties of Gallium Citrate. *J. Am. Chem. Soc.* In press, 1950.
  6. DUDLEY, H. C., BRONSON, J. F., AND TAYLOR, R. O.: Shielding of Syringes Used for Injecting Radioactive Solutions. *Science* **110**: 16-17, July 1, 1949.
  7. CRISP, L. R. Personal communication. National Institutes of Health, Bethesda, Md.
  8. BÉLANGER, L. F., AND LEBLOND, C. P.: Method for Locating Radioactive Elements in Tissues by Covering Histological Sections with a Photographic Emulsion. *Endocrinology* **39**: 8-13, July 1946.
  9. HAYNES, S. K.: Beta and Gamma Spectrum of  $Ga^{72}$ . Atomic Energy Commission. MDCC 1686, 9 Feb. 1948.
- Naval Medical Research Institute  
Bethesda 14, Md.

## SUMARIO

Depósito de Radiogallio ( $Ga^{72}$ ) en los Tejidos Proliferantes

Según se observó, el radiogallio ( $Ga^{72}$ ) se concentra en las zonas de actividad osteógena, por ej., la unión epifisaria y el callo de las fracturas en vías de cicatrización en los conejos y el sarcoma osteógeno del ratón. En ciertos fibroadenomas, fibrosarcomas y tumores mamarios mixtos de los animales, no hubo localización significativa de  $Ga^{72}$ .

Los estudios autorradiográficos del de-

pósito de  $Ga^{72}$  en el hueso, por medio de la impregnación de cortes óseos con emulsión fotográfica líquida, ha permitido localizar con mayor precisión el elemento mencionado.

Sugiere que el citrato de radiogallio ( $Ga^{72}$ ) es acreedor a pruebas clínicas, en cantidades indicativas para fines de diagnóstico y a dosis mayores por su posible efecto terapéutico.

# Radiation-Induced Mutations in Mammals<sup>1</sup>

DONALD R. CHARLES, Ph.D.

Rochester, N. Y.

THERE ARE TWO particular questions about radiation-induced mutations in mammals which should be of interest to radiologists: (1) How likely are mutations to occur, as a function of dose? (2) How serious are their effects?

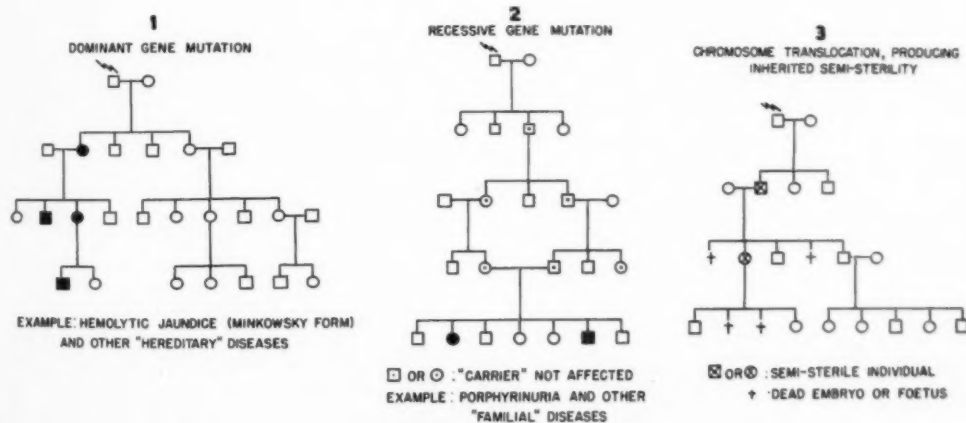
Let us first remind ourselves of the main classes of mutations recognized by geneticists. Figure 1 shows a hypothetical pedigree involving a *dominant gene mutation*; Figure 2 represents a *recessive gene mutation*, and Figure 3 an inherited semi-sterility caused by a *chromosome translocation*. How frequently such changes occur in mammals as a result of exposure to radiation is still far from accurately known. The published data, all obtained from mice (Table I) indicate that, for single large exposures, inherited semi-sterilities are the main genetic effect to be expected, occurring in a small percentage of sperm for each 100 r. The gene mutation rates are not very reliable, since they are calculated from a few mutations in a small number of tested cells (Table II).

TABLE I: RADIATION INDUCED MUTATIONS REPORTED IN MICE

Type of Mutation	Mouse Mutation Rates, per 100 r		Neutrons, Snell
	X-rays Hertwig	Snell	
Chromosome translocation, producing inherited semi-sterility	2-3%	5%	7-9%
Gene mutations			
Dominant, structural	<0.3%	0.2%	<4%
Recessive, structural	0.4%	<1%	<7%
Recessive lethal	? %	<4%	?
Dose used	400-1,600 r	600 r	110-140 r eq.

For practical applications, one would like to know something about mutation rates under *repeated small exposures* to penetrating radiation. Such data were obtained at the University of Rochester Atomic Energy Project between 1943 and the present. They are summarized in Table III.

These results may be compared with those of the previous investigators for single doses (Table IV). Both the disagreements in chromosome mutation rate



Figures 1-3

<sup>1</sup> From the University of Rochester, Rochester, N. Y. Presented before the Thirty-fifth Annual Meeting of the Radiological Society of North America, Cleveland, Ohio, Dec. 4-9, 1949.

TABLE II: MUTATIONS FOLLOWING SINGLE LARGE EXPOSURES TO RADIATION

Type of Radiation	Cells Exposed	Type of Change Tested for				Investigator
		Chromosome Translocation Producing Semisterility	Gene mutations			
			Dominant Affecting Structure	Recessive Affecting Structure	Recessive Lethal	
X-rays: 600 r	Mature sperm in ducts	38/114	1/91	0/50	0/10	Snell 1935
X-rays: 400-1,600 r	Mature sperm and eggs	43-64/263	..	..	..	Hertwig 1940
X-rays: 600-1,600 r	All stages in sperm development	.....	0/96	4/96	..	Hertwig 1939
Neutrons: 110-140 r equiv.	Mature sperm in ducts	4-5/47	0/67	0/33	..	Snell 1939
Total mutations found		85-107		5		
Total gametes tested		424		254		

TABLE III: MUTATIONS FOLLOWING REPEATED SMALL EXPOSURES TO RADIATION

r/Exposure,	Number of exposures				Average Total Exposure (r)	Total Sperm Normal	Found to be Carrying			Per Cent of Sperm with a Mutation	
	1-99	100-199	200-299	300-399			T	1	G*		
	Number of Sperm Tested,						0	2	1		0
0		2,755				0	2,752	2	1	0	0.11
0.1	592	465	303	106	13	1,461	1	0	4	0.34	
0.5	358	347	232	64	69	995	2	2	2	0.60	
1.0	160	175	102	17	134	451	2	0	1	0.66	
10	151	...	...	...	238	149	2	0	0	1.32	

Induced Mutation Rate:

$$\frac{(16/3,072) - (3/2,755)}{60} = 7 \times 10^{-6} \text{ per sperm per r or } 0.007\% \text{ of sperm mutating per r.}$$

\* T. Semi-sterility mutations. 1. One class of recessive mutations. G. Dominant gene mutations.

and the agreement in dominant gene mutation rate are to be expected from the results of many workers with plants and insects. In those organisms, the gene changes depend only on total dose, no matter how spaced in time; the chromosome changes depend very strongly on dosage rate. Hence we may take the lower (University of Rochester) value as more nearly applicable to human tolerance problems.

TABLE IV: PERCENTAGE OF SPERM MUTATING PER 100 R

	Chromosome Mutation	Dominant Gene Mutation
Single dose (400-1,600 r)	2-3; 5	0.2
Repeated small doses (0.1-10 r)	0.4	0.3

Let us now turn to the question: How serious are the effects of radiation-induced mutations? Our basis for judgment—so

far as gene mutations are concerned—is very scanty. The types of change may be listed as follows:

1. Retarded growth (Hertwig)
2. Anemia, early death (Hertwig)
3. Oligodactyly, early death (Hertwig)
4. Abnormal spleen shape (Snell)
5. Abnormal connections of minor tributaries of vena cava (Charles)
6. Extra nodules of adrenal cortical tissue (Charles)
7. Incomplete suture of parietal bones (Charles)
8. "Confused" behavior, occasional cataract and deafness (Charles)
9. Reduced eye size and fertility, altered fur color (Charles)
10. Altered fur color (Charles).

Of the twelve mutations, perhaps only 7 show clearly adverse effects, but it is the general impression of geneticists, I believe, that most mutant genes, when adequately studied, are found to be harmful.

We know somewhat more about the

semi-sterility mutations. Six have been studied so far, by dissection of semi-sterile females (or of females mated to semi-sterile males) at various intervals after timed matings. In all six semi-sterilities the embryos have been dead before the thirteenth day.

One would like to know what would be the death time for comparable mutation occurring in man. We have attempted an answer by studying the time equivalence between mouse and human development (Fig. 4). We are led to conclude tentatively that women with inherited semi-sterility would lose half of their offspring in the embryonic period, before the seventh week, and so presumably without really serious effects.

In summary, new mutations occur in about 1 per cent of mouse sperm for each 100 roentgens exposure at low-dosage rate. Of these mutations, about 40 per cent would perhaps not be a real health hazard to individuals inheriting them. Another 40 per cent—the recessives—would not be apparent for probably many generations. Only 20 per cent—the dominants—would have immediate effects on offspring receiving them.

	Mutation rate
Chromosome translocations.....	0.4% per 100 r
Recessive gene mutations.....	0.4%
Dominant gene mutations.....	0.3%
Total.....	1.1%
"Significant" total over few generations.....	0.3%
"Significant" total over many generations.....	0.7%

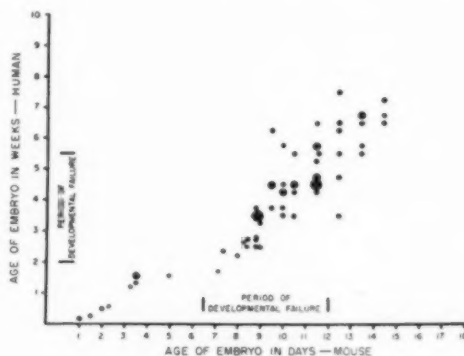


Figure 4

If we use these values in estimating the consequences of various amounts of radiation impinging on various proportions of a human population, we must remember that our answers may be quite inaccurate for two reasons: (1) Statistical and systematic errors in the mouse mutation rates based, as they are, on small numbers of mutations; (2) possible differences in radiation sensitivity between mouse and human chromosomes.

University of Rochester  
Rochester 3, N. Y.

#### REFERENCES

- HERTWIG, P.: Zwei subletale rezessive Mutationen in der Nachkommenschaft von röntgenbestrahlten Mäusen. *Erbarzt* 6: 41-43, 1939; Vererbare Semi-sterilität bei Mäusen nach Röntgenbestrahlung, verursacht durch reziproke Chromosomtranslokationen. *Ztschr. f. indukt. Abstammungs- u. Vererbungslehre* 79: 1-27, 1940.
- SNELL, G. D.: Induction by X-rays of Hereditary Changes in Mice. *Genetics* 20: 545-567, 1935; Induction by Irradiation with Neutrons of Hereditary Changes in Mice. *Proc. Nat. Acad. Sc.* 25: 11-14, 1939.

#### SUMARIO

##### Mutaciones Evocadas por la Radiación en los Mamíferos

Por cada exposición a 100 roentgens a baja dosis sobrevienen mutaciones aproximadamente en 1 por ciento de los espermátides murinos. De esas mutaciones, aproximadamente 40 por ciento quizás no constituyan un riesgo real para la salud del individuo que las herede. Otro 40 por ciento—las mutaciones recesivas en los genes—probablemente no se hará sentir por muchas generaciones. Sólo un 20 por ciento—las mutaciones dominantes en los

genes—ejercería efecto inmediato en la prole que las reciba.

La aplicación de esas cifras al cálculo de las consecuencias de diversas cantidades de irradiación en varias proporciones de una población humana puede dar resultados bastante inexactos, debido a: (1) errores estadísticos y sistemáticos en los coeficientes de mutación murina, y (2) posible diferencia en la radiosensibilidad de los cromosomas murinos y humanos.

## Telognosis<sup>1</sup>

J. GERSHON-COHEN, M.D., and A. G. COOLEY

Philadelphia, Penna.

THE TERM "telognosis" is used to abbreviate the three terms—"teleo roentgen diagnosis"—indicating roentgenographic diagnosis obtained from facsimiles of original roentgenographs transmitted by radio or telephone wires over short or long distances.

More and better hospitals are the aim not only of small rural communities, but

lem of rapid long-distance transmissions of picture facsimiles over commercial telephone wires and there seemed to be some reason to believe that a similar service could be developed for roentgenography.

### DESCRIPTION OF APPARATUS

This system of long-distance roentgenographic facsimile *via* commercial tele-

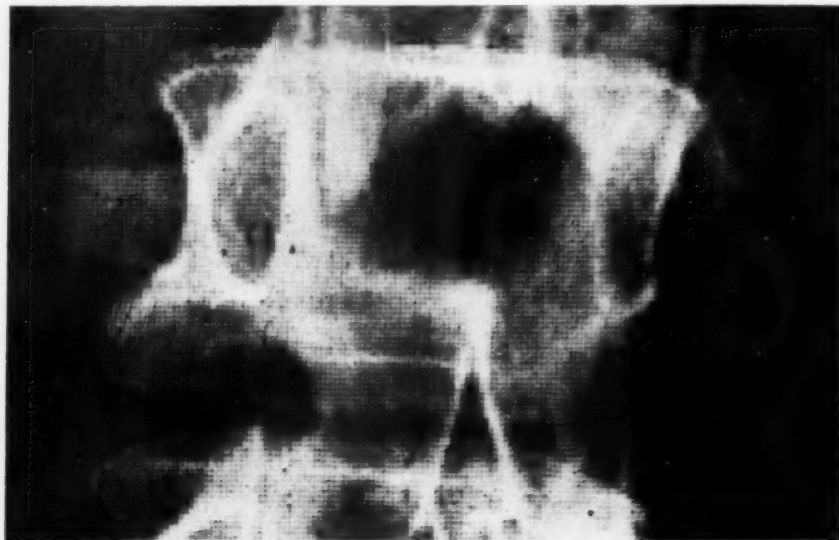


Fig. 1. Magnified facsimile to show elemental areas of photographic exposure.

also of the medical profession and government alike. One of the most difficult problems raised in the functioning of a good rural hospital is the successful operation of a clinical and x-ray laboratory. At present, the part-time attendance of an experienced radiologist from the nearest large urban center is secured, but this arrangement necessitates waste of much time in travel, sometimes over long distances. The newspaper services solved the prob-

lem of rapid long-distance transmissions of picture facsimiles over commercial telephone wires and there seemed to be some reason to believe that a similar service could be developed for roentgenography.

The transmitting equipment (Fig. 2) consists of a glass drum around which film of any dimensions, up to 14 × 17 inches, can be clamped in place. This cylinder is 5 inches in diameter and 18 inches long. It rotates at a uniform speed of 180 r.p.m., while a small beam of light is

<sup>1</sup> Accepted for publication in February 1950.

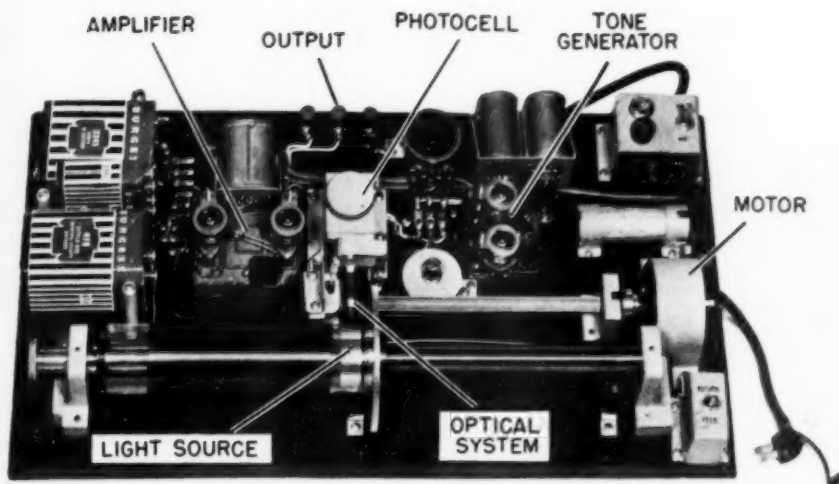


Fig. 2. Roentgenographic facsimile transmitter.

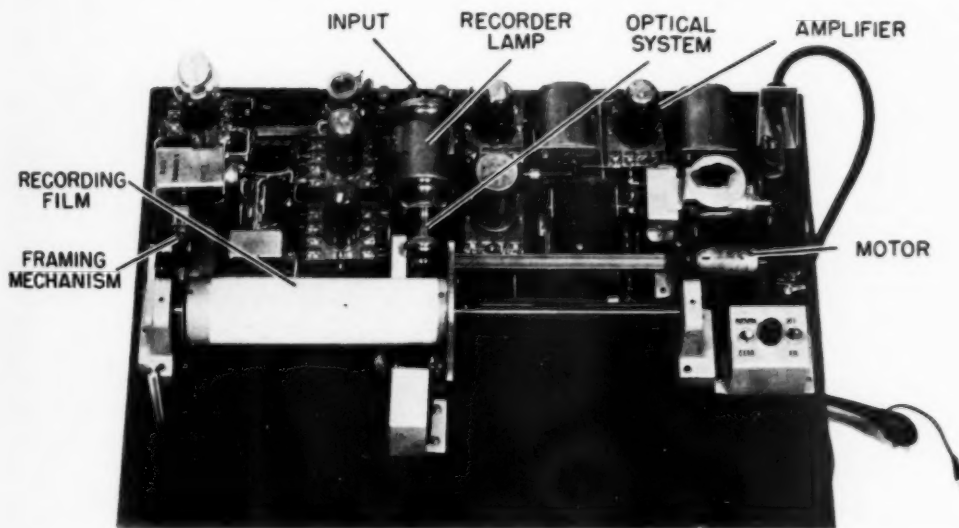


Fig. 3. Roentgenographic facsimile recorder.

focused onto the film. The illuminated or elemental area measures  $1/50$  of a square inch (Fig. 1). Light passing through the film is picked up by a photocell inside of the glass cylinder. This photocell is connected with a pre-amplifier for building up the picture signal before it is passed on to an output amplifier connected to the telephone line or radio transmitter. Over a

modern voice frequency circuit, 2,700 elemental areas can be transmitted per second. This corresponds to approximately one square inch of the original x-ray film. Under normal operating conditions, a  $14 \times 17$ -inch film is transmitted in four and one-half minutes. Smaller films can be transmitted in correspondingly less time. Several smaller films can be transmitted at

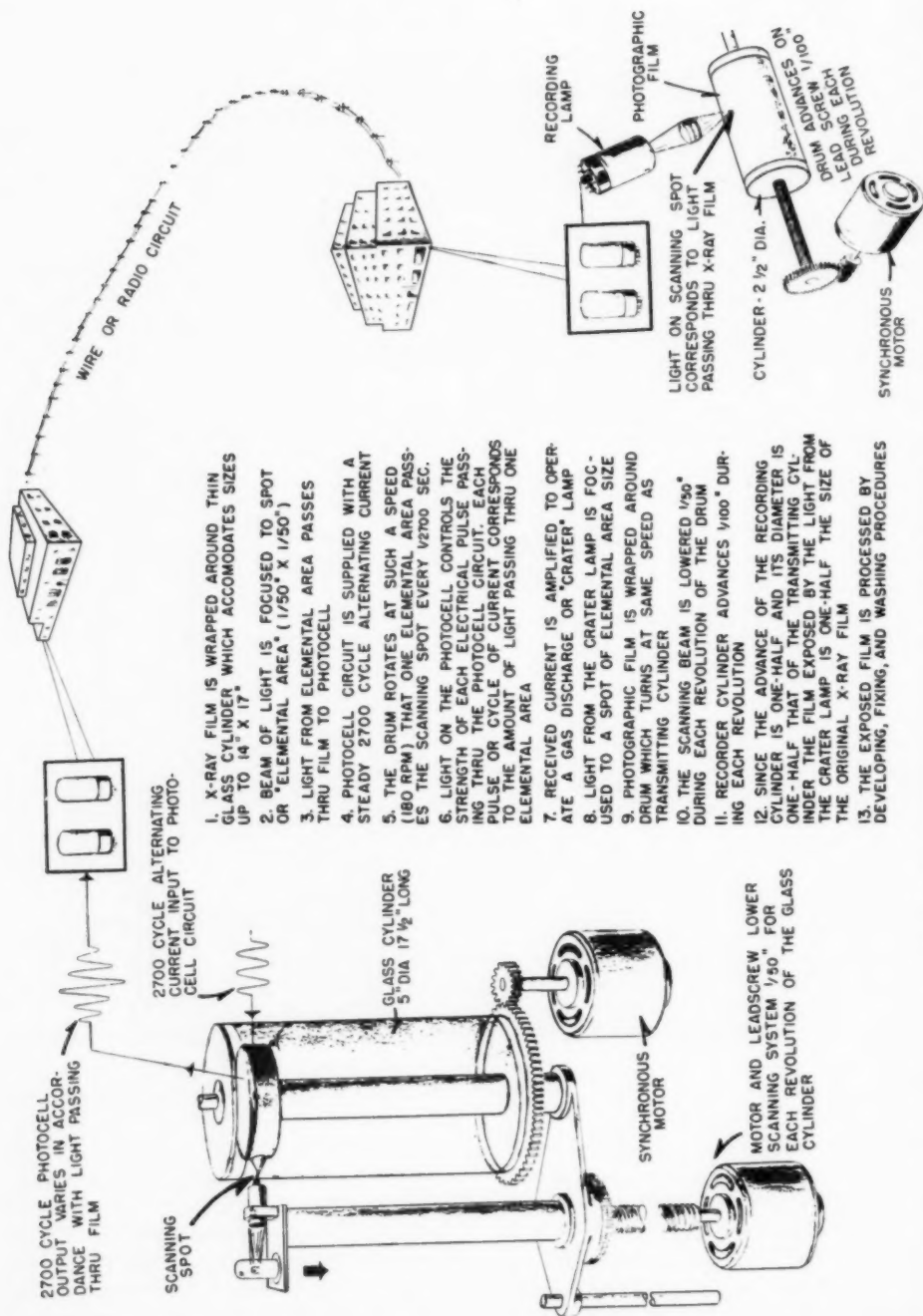


Fig. 4. Diagrammatic illustration of facsimile transmission.

the same time by combination on the transmitting cylinder.

After the 2,700 cycle tone is fed into the photocell circuit, the light on the photocell modulates the tone so that the output to the pre-amplifier varies in amplitude in accordance with the light passing through the film. The strength of the signal into the telephone circuit is the same as the signal produced by an ordinary telephone voice transmitter.

The receiving equipment (Fig. 3) includes a cylinder  $2\frac{1}{2}$  inches in diameter, which is one-half the size of the transmitting cylinder. Wrapped on this cylinder is a photographic film made by Eastman Kodak Co. for this type of transmission, called Type C. A small beam of light is projected upon this film, corresponding in intensity and size to the light which passes through the x-ray film at the transmitter. The light at the recorder comes from a glow-discharge lamp sometimes called a "crater lamp."

This receiving cylinder rotates at a uniform speed of 180 r.p.m., synchronously with the transmitting cylinder. During each revolution, while the scanning mechanism of the transmitter is advanced one-fiftieth of an inch, that of the recorder is advanced one one-hundredth of an inch, i.e., there are 50 scanning lines per inch at the transmitter and 100 at the receiver. Since the recording cylinder is half the diameter of the transmitting cylinder, the facsimile is one-half the size of the original roentgenogram. The recording is in the form of square elements one one-hundredth of an inch on a side. These elements blend together so that it is difficult to distinguish them without a magnifying glass.

After the recording film has been exposed, it may be developed and fixed in the same solutions used for roentgenograms, but the time of processing is almost one-half of that necessary for ordinary x-ray films. This special recording film is hardy, and will stand considerable abuse. It can be developed in concentrated developer in less than one minute, and it also can be fixed in less than one minute in con-

centrated fixing solution. The processing time could be reduced still more by use of warm solutions. With modern drying apparatus, a dried facsimile can be had in four minutes after recording. Since the original film is retained at the transmitting point, it really is not necessary to process the received film for permanency. A one-half minute wash is sufficient if the received film is not needed for more than one week.

The design of the equipment now in operation between West Chester and Philadelphia had the advantages of the designer's (A.G.C.) experience with building similar equipment for wire photo transmission, and this already had been brought to a high state of efficiency before research on the present design was begun. During World War II, wire photo telegraph transmitters were in operation between Washington, D. C., and Anchorage, Alaska. Other radio circuits operated between Antarctica and Washington, D. C. It is therefore expected that after some additional field trials of improved roentgenographic models, equipment for practical long distance wire or radio transmission will be obtainable.

#### COMMENTS

The test apparatus in use has required little servicing during the past year, and the actual transmission and reception technics have been carried out by the staff roentgen technician or by one of the developing room personnel. There has been no instance where a diagnosis from the facsimile was in error because of impaired detail in the reproduction. As a matter of fact, because the facsimile is one-half the size of the original film, many details are sharper than in the original. For this reason, fracture lines sometimes are seen more easily in the facsimile.

Under our present arrangement, there are full-time radiologists on duty at the Chester County Hospital, so that seldom has there been a necessity for emergency use of the facsimile equipment. Several times during the absence of the hospital staff radiologist, some rather dramatic experi-

Fig. 4. Diagrammatic illustration of facsimile transmission.



Fig. 5. Original roentgenogram of acute sigmoidal volvulus seen at Chester County Hospital, West Chester, Penna. The transverse line across the middle of the film is due to a cut necessitated by the small drum of the experimental model, which transmits no film larger than  $10 \times 12$  inches, so that only half of a  $14 \times 17$ -inch film can be transmitted at one time.

ences have been encountered. On one such occasion, a prominent patient was admitted with acute abdominal symptoms, and the surgeon, Dr. C. Kerwin, desired an emergency x-ray consultation. Facsimiles of the original abdominal films were available in Philadelphia a few minutes after the latter were obtained in West Chester, and these facsimiles disclosed the presence of a large bowel obstruction, probably due to volvulus of the sigmoid. With this diagnosis, so quickly obtained over the same telephone circuit that provided the facsimiles, the surgeon proceeded to an immediate operation. The diagnosis was confirmed, and the operation was successful. This kind of experience has been repeated many times with other members of the hospital staff, and naturally this has led to confidence in the reliability of the procedure. We have had sufficient experience with this first experimental model during the past two years to venture the prediction that, if and when this service can be supplied at low enough cost, it will become a useful tool for the small rural hospital in obtaining full-time expert radiologic service for its staff.

#### SUMMARY

"Telognosis" (abbreviating "teleoroentgen diagnosis") is a diagnostic procedure utilizing x-ray film facsimiles obtained by transmission over radio or telephone wire circuits. This facsimile procedure can supply expert roentgenologic service to the staff of a distant rural hospital without the necessity of a roentgenologist moving from his main center of activity. Experimental



Fig. 6. Facsimile of original film shown in Fig. 5, which was transmitted over a telephone circuit to Philadelphia, from the Chester County Hospital x-ray laboratory, where the patient was examined. Consultation between the roentgenologist and surgeon, twenty-eight miles apart, took place over the same telephone circuit, with no more delay than a similar consultation would entail with the surgeon and roentgenologist present together in the hospital.

apparatus has been in daily operation for two years between Chester County Hospital and Philadelphia, Penna. Engineering improvements are now being pursued to reduce the cost sufficiently to make this procedure economically practicable.

255 S. 17th St.  
Philadelphia 3, Penna.

#### SUMARIO

##### Telognóstico

El telognóstico (abreviatura de teleoroentgenodiagnóstico o diagnóstico teleoroentgenológico) es un procedimiento diagnóstico que utiliza facsímiles roentgenográficos obtenidos por transmisión por circuitos radio o telefónicos. El aparato y la técnica aparecen aquí descritos e ilustrados.

Este procedimiento ha sido empleado sistemáticamente durante un período de dos años a través de una distancia de unos 28 km., entre el Hospital del Condado Chester y la ciudad de Filadelfia, sin cometer en ningún caso errores de diagnóstico debido a menoscabo de los detalles en el facsímile.

## Clinical Cinefluorography<sup>1</sup>

ROBERT F. RUSHMER, M.D., RAYMOND S. BARK, and JOHN A. HENDRON

Seattle, Wash.

SINCE THE DISCOVERY of the roentgen rays, utilization of roentgenography has been progressively diversified by improvements in apparatus and technic. The possibility that motion pictures might be taken of a fluorescent screen was recognized by MacIntyre (1897) who synthesized from a series of roentgenograms a film revealing motion of a frog's hind leg. Subsequently, motion picture photography of the fluorescent screen has been successfully accomplished by a number of investigators (1-14). Despite the advantages offered by cinematic recording of fluoroscopic images, surprisingly little attention has been directed toward the use of cinefluorography as a routine diagnostic aid. Moretzsohn de Castro (10) in São Paulo, Brazil, and Ramsey and co-workers (13) in Rochester, N. Y., report progress in adding this method to the diagnostic armamentarium. The former emphasized studies of gastro-intestinal disorders, and the latter have concentrated on syndesmology and swallowing.

The exposure of patients to x-radiation and the capacity of x-ray tubes impose strict limitations on the duration of motion picture recording. The cinefluorographic technic appears peculiarly adaptable to the study of the cardiovascular system, where rapid and repetitive motion is intimately related to function and where the flow of radiopaque materials can be adequately studied only by means of a permanent record. To this end, cinefluorographic equipment has been developed for specialized studies of the circulation in health and disease.

### APPARATUS

Simple cinefluorographic apparatus has indicated the practical usefulness of cine-

matic fluorography (14). On the basis of this experience, improved equipment has now been designed for the routine study of selected patients, particularly with congenital heart disease. Increased versatility was sought by mounting the cinefluorographic equipment to permit efficient operation in either the vertical or horizontal position. A standard motor-driven, tilting fluoroscopic table was converted to this purpose (Figs. 1 and 2). The fluoroscopic attachments were removed, and the inside of the table was lined with sheet lead to restrict secondary radiation and to render the interior light-tight. The Potter-Bucky diaphragm was replaced by a frame supporting both a Patterson E-2 screen and a front surface mirror inclined 45° toward the camera (Fig. 2). The frame, supporting the screen and mirror, moves freely along a track just beneath the table top but can be locked at any one of five positions. At varying distances from the fluorescent screen, the camera, equipped with an f 0.8 coated 50-mm. lens, photographs areas ranging from 5 × 6 to 10 × 12 inches.

The exposure of patients to radiation is the primary consideration in determining the duration of cinefluorographic recording. An arbitrary value of 20 r has been selected as the maximum dose to which patients are routinely exposed. This self-imposed limitation necessitates efficient operation in every stage to obtain satisfactory results.

For example, the shutter in most motion-picture cameras is closed approximately 50 per cent of the time. By interrupting the generation of x-rays while the film is being advanced, the exposure can be reduced by half, or a twofold increase in the duration of cinefluorographic recording can be obtained without increasing the exposure of the patient to radiation. This problem

<sup>1</sup> From the Department of Physiology and Biophysics, University of Washington, Seattle, Wash. Accepted for publication in January 1950.

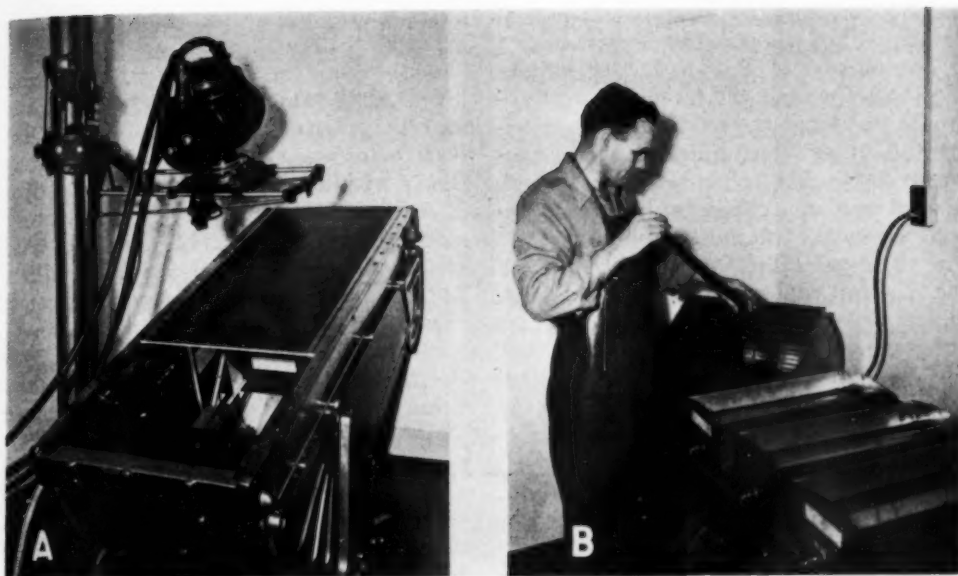


Fig. 1. A. Cinefluorographic equipment has been installed in a motor-driven, tilting x-ray table. The 35-mm. camera is directed toward a front surfaced mirror, supported at  $45^\circ$  by a metal frame. A fluorescent screen, mounted just beneath the table top on this frame, can be seen in the reflection from the mirror.

B. The film is processed on a stainless steel reel, rotating within a metal hood which is inverted over each of the solution trays.

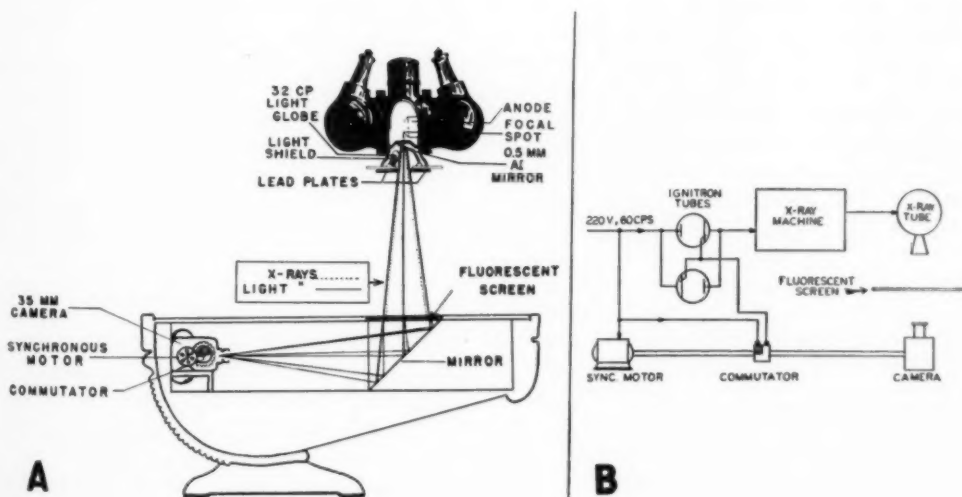


Fig. 2. A. The x-ray beam size is limited by adjustable lead plates and is localized by visible light from a 32-candlepower globe reflected through the same aperture. Under the influence of x-rays, the fluorescent screen emits visible light which reflects from a front surfaced mirror into the motor-driven camera. A commutator with 180° segments, fastened to the drive shaft of the camera, synchronizes the x-ray output with the advancing mechanism in the camera.

B. The block diagram indicates the circuit by which the commutator, activating the ignitron tubes, allows current to flow into the x-ray generator only when the camera shutter is open.

of synchronizing the x-ray machine and motion-picture camera has been attacked in several ways (1, 2, 3, 6, 11, 12). Since each had apparent limitations, a new approach was made to accomplish this refinement. Full-wave rectified machines produce 120 pulses of x-ray per second. A short persistence fluorescent screen, illuminated by the intermittent x-ray output, can be successfully photographed only if each frame is exposed to precisely the same number of pulses. Therefore, the shutter speed must be carefully synchronized with the x-ray output. Specifically, a switch was required which would rapidly and precisely interrupt the heavy current supplying the transformer of a General Electric KX-1 x-ray machine with CRT 1-2 tube.<sup>2</sup> Accurate synchronization was obtained by the mechanism described below.

A commutator and the advancing mechanism of a 35-mm De Vry camera are both connected to a shaft, driven at a rate of 15 revolutions per second by means of a synchronous motor. The commutator is adjusted to close a circuit only while the camera shutter is open (Fig. 2B). This circuit activates a heavy-duty electronic switch (General Electric ignitron contactor, type CR7503-E) which controls the flow of current to the x-ray generator. With this mechanism, each frame is exposed to light generated by four pulses of x-ray and the flow of current is interrupted during the next four pulses while the film is advanced. It should be noted that ignitron contactors produce a constant voltage drop of 15 volts in the line to the x-ray transformer. Compensation can be readily made by adjusting the kv.p. control. Ignitron tubes are particularly suited to this application for the following reasons: (1) The switching is virtually instantaneous. (2) Precise control is facilitated because an ignitron will sustain conduction to the end of a half cycle of the alternating current. (3) Ignitron contactors will handle heavy current without the arcing or the

other undesirable characteristics of mechanical switches.

With this system, the synchronization between the camera and x-ray generator is so reliable that the camera shutter has been completely removed without interfering with the results. A film speed of 15 frames per second is used for circulatory studies, but film speeds of 30 or 60 frames per second can be readily obtained with a suitable gear ratio on the drive motor.

Further reduction in the exposure of patients to radiation is accomplished by a device which accurately restricts the x-ray beam to the area being photographed (Fig. 2A). The adjustable lead shutter from a fluoroscopic tube was adapted to the CRT 1-2 x-ray tube casing so that a rectangular orifice of variable dimensions could be formed. A 32-candlepower light was mounted behind the lead shutter, and a polished aluminum mirror (0.5 mm. thick) was adjusted so that visible light from the lamp passes through the orifice formed by the lead plates and precisely outlines the area which will be covered by the x-rays. With the device, the relation between the tube, patient, and screen can be assured under direct visual observation.

Processing the exposed film in the laboratory is readily accomplished and provides several advantages: (1) The film can be developed and prepared for projection within two hours, if necessary. (2) Testing of films, exposure factors, and equipment can be greatly facilitated. (3) It is not necessary to expose an entire roll of film before developing. (4) The cost is moderate and (5) the results are consistently better than those obtained from commercial concerns. Satisfactory film processing equipment has been constructed in the University shops (Fig. 1B). A reel composed of stainless steel rods is mounted in a metal hood and slowly rotated at constant speed by an electric motor. The hood is placed successively over three stainless steel trays which contain sufficient processing chemicals to cover the film at the bottom of the reel. This system permits carefully controlled development with gen-

<sup>2</sup> This equipment was generously donated for the project by the General Electric X-ray Corporation.

the agitation, but without waste of chemicals or abrasion of the emulsion. When the hood is correctly placed over the trays, the film is protected from incident light so that a major portion of the process can be conducted in a dimly lighted room.

#### APPLICATIONS OF CINEFLUOROGRAPHY

The ability to discern objects is facilitated if they are in motion. Just as a bird with brilliant plumage may remain undetected until it moves, so the slight differences in intensity in roentgenographic images become emphasized in x-ray motion pictures. A rapidly moving shadow attracts attention more readily than a slowly moving one. For example, it has been possible to observe cardiac borders which are superimposed upon the spine shadow during projection of the films, while the same difference in density is difficult to distinguish on individual frames. This feature is singularly valuable in observing the activity of the left ventricular border in the left anterior oblique position. The localization and orientation of bronchovascular markings become apparent if the exposure is made during respiratory activity or while the patient is being rotated. Most revealing are the films made while rotating the patient from the postero-anterior position into the left anterior oblique position and back. A distinct three-dimensional impression of the thorax is gained from these films, because the shadows in front of the axis of rotation move in one direction, while those behind move in the opposite direction. The change in the cardiac contour, as various aspects come into view, aids in visualizing the components of the cardiac silhouette in various positions.

Cinefluorography is a valuable adjunct in research and diagnosis. Currently, the technic is being used for the following purposes: (1) Changes in the cardiac silhouette during cardiac contraction are being studied by tracing consecutive frames of selected films. (2) Permanent records of the fluoroscopic appearance of the heart

are being obtained in cases of congenital and acquired heart disease. (3) The movements of normal and abnormal joints have been recorded. (4) The course of a swallow of barium has been photographed, and the impact of the left auricle on the esophagus is being studied. (5) Training films, demonstrating the fluoroscopic appearance of the cardiac silhouette, have been prepared (14). (6) Motion pictures revealing the course of diodrast through the right heart have been obtained on five patients. Technical refinements are being developed on experimental animals so that cinematic angiocardiology can be undertaken as a diagnostic procedure in suitable cases. Indeed, the improved equipment described above was designed primarily for angiography and angiocardiology. Additional applications are limited only by the restrictions imposed by the exposure of the subjects to radiation and the ingenuity of the investigator.

Cinefluorography of the heart can be accomplished with less total radiation than is used in certain routine roentgenographic procedures. During fluoroscopy, the patient is exposed to about 25 r/min. over an area regulated by the observer. If the films can be projected in lieu of repeated fluoroscopic examinations, the exposure of any particular patient can be effectively reduced. With respect to intensity, contrast, and detail, the projected images are superior to the shadows observed during routine fluoroscopy. Further, the permanent record of the fluoroscopic appearance of a heart seems superior to a verbal description of the direct observation.

#### SUMMARY

Apparatus for cinematic recording of fluoroscopic images has been designed for clinical application. The use of ignitron contactors to synchronize the camera and the output of the x-ray tube is a new approach to the problem of reducing the exposure of patients to radiation during this procedure. The advantages of cinefluorographic recording as a diagnostic aid have not been fully realized.

## REFERENCES

1. REYNOLDS, R. J.: Cineradiography. *Brit. J. Radiol.* **7**: 415-424, 1934.
2. REYNOLDS, R.: Cineradiography by the Indirect Method. *Radiology* **31**: 177-182, 1938.
3. JANKER, R.: Roentgen Cinematography. *Am. J. Roentgenol.* **36**: 384-390, 1936.
4. FRANKLIN, K. J., AND JANKER, R.: Respiration and Venae Cavae—Further X-ray Cinematographic Studies. *J. Physiol.* **86**: 264-268, 1936.
5. FRANKLIN, K. J., AND JANKER, R.: Coughing Studied by Means of X-ray Cinematography. *J. Physiol.* **92**: 467-472, 1938.
6. KAWAISHI, K.: Studies on Roentgen Cinematography of the Internal Organs and Circulation of the Blood of the Human Body. *Am. J. Roentgenol.* **40**: 913-921, 1938.
7. STEWART, W. H., HOFFMAN, W., AND GHISELIN, F. H.: Cinefluorography. *Am. J. Roentgenol.* **38**: 465-469, 1937.
8. STEWART, W. H., AND GHISELIN, F. H.: Recent Developments in the Cinematography of the Fluoroscopic Image. *South. M. J.* **30**: 268-270, 1937.
9. BARCLAY, A. E., FRANKLIN, K. J., AND PRICHARD, M. M. L.: X-ray Cinematography in Research. *Brit. J. Radiol.* **13**: 227-234, 1940.
10. MORETZSOHN DE CASTRO, J.: Fundamental Principles in the Application of Cincroentgenography as an Auxiliary Method to Roentgen Diagnosis. *Am. J. Roentgenol.* **57**: 103-114, 1947.
11. REHMAN, I.: High Speed X-ray Motion Picture Studies. *J. Biol. Photographic A.* **16**: 15-21, 1947.
12. WATSON, J. S., JR., AND WEINBERG, S.: A 35-Mm. Unit for Cinefluorography. *Radiology* **51**: 728-732, 1948.
13. RAMSEY, G. H. S., WATSON, J. S., JR., STEINHAUSEN, T. B., THOMPSON, J. J., DREISINGER, F., AND WEINBERG, S.: Cinefluorography: A Progress Report on Technical Problems, Dosage Factors and Clinical Impressions. *Radiology* **52**: 684-690, 1949.
14. RUSHMER, R. F.: Cinefluorography of the Normal Human Heart; Teaching Application. *Fed. Proc.* **8**: 136, 1949.

Schood of Medicine  
University of Washington  
Seattle 5, Wash.

## SUMARIO

## Cinefluorografía Clínica

Este aparato para el registro cinematográfico de las imágenes roentgenoscópicas está destinado a empleo en la clínica. El uso de contactores de ignitrón para sincronizar la cámara y la emisión del tubo de rayos X constituye una nueva solución del problema de reducir la exposición de los enfermos a la irradiación durante este procedimiento. Se logra otra reducción en la exposición por medio de un dispositivo que circunscribe con exactitud el haz de rayos

X a la zona en vías de ser fotografiada. Ya se ha construido una instalación satisfactoria que permite atender prontamente a la película expuesta en el laboratorio y preparar la proyección en dos horas.

El equipo descrito estaba primordialmente destinado a la angiografía y la angiocardiógrafía. Recálcse que no se han comprendido aun plenamente las ventajas que ofrece el registro cinefluorográfico como auxiliar en el diagnóstico.



# EDITORIAL

## The Nasopharyngeal Applicator

Clarification of some of the problems associated with the nasopharyngeal "beta" radium applicator (content 50 mg.; active length 1.6 cm.; diameter 2.3 mm.; 0.3 mm. Monel wall; about 70 per cent beta and 30 per cent gamma radiation at the surface) may be needed because of the findings of Braestrup (1) in a recent article on the ionization measurements of the tissue doses in equivalent roentgens. This applicator has been used by otolaryngologists for treatment of hypertrophied lymphoid tissue in and about the eustachian orifices on a more or less empirical basis, without satisfactory knowledge of the doses delivered to the tissues. Earlier dosage estimates varied considerably and their authors made no claims for their accuracy. However, the calculated values of Quimby (2) were in close agreement with the experimental values of Braestrup.

The value of the applicator in the treatment of some benign nasopharyngeal and otic conditions is recognized. At least 2,000 of these applicators are in use in the United States and Canada today in treating excessive lymphoid tissue around the eustachian tubes to combat deafness by eliminating sequelae of chronic infections of the middle ear. This form of therapy is accompanied by the usual risks inherent in the use of radium and is, of course, potentially dangerous to the patient as well as to the physician and his staff.

To determine the exposures received by patients and personnel, Rubin *et al.* (4) have shown, in a carefully monitored series of treatments, that total body irradiation did not exceed six milliroentgens per treatment for the physician and assistant. The permissible dose for the whole body is three hundred milliroentgens per week.

However, the average exposure for the entire length of both index fingers of the physician was twenty-six milliroentgens and of several finger tips fifty milliroentgens per treatment. The maximum number of treatments which one physician may administer weekly is twelve, finger tip and not whole body exposure being the limiting factor. Lead shields or other accessories for the applicator, or modification in its construction, such as lengthening the handle, will reduce the exposure to the physician's finger tips and permit a greater number of treatments. These studies indicate that it would be well to monitor every physician's technic to determine the number of treatments he may administer without exceeding the permissible value.

If the standard applicator is used with the recommended precautions, there is little likelihood of any serious damage. Crowe and his associates (3) have had a wider experience with this type of therapy than any other group in this country. They say: "Irradiation of adenoid tissue has now been used for twenty-four years and many thousands of patients have been treated. In all this time not a single instance of burn or other complication due to the use of radium has been observed." So far no serious complication has been reported from any other clinic where this method has been used for shorter periods. Occasionally a transient catarrhal otitis media has been noted by some observers. Constant vigilance must always be maintained because radiologists better than other specialists realize the potential dangers and are in a position to assist and to warn their colleagues. Anyone who employs this form of radium therapy assumes a serious responsibility, but because a good

method is occasionally misused, the whole procedure should not be condemned. In fact, an attempt can now be made to apply it more intelligently.

There probably is a physical explanation for the fact that a visible reaction rarely occurs in the nasopharynx, namely distance. Using a nasopharyngoscope in the opposite nostril for accurate placement, tying the ends of the applicators together to spread the other ends as far apart as possible, and shrinking the turbinates before irradiation, are methods of obtaining closer contact, but they are not routinely employed. According to Braestrup's measurements, a twelve-minute exposure, which is the one customarily used, delivers 4,440 equivalent roentgens in contact with the center of the tube but only 60 gamma roentgens at one centimeter depth. Hyperplastic lymphoid tissue tends to form irregular nodules about the eustachian orifices, so that only a small part of the applicator, say two or three millimeters, may be in actual contact with the apex of a nubbin of tissue, whereas the rest of it may be three or four millimeters away. This latter part of the surface will receive only 696 or 432 equivalent roentgens, and any that is farther away will receive considerably less because the drop in depth dosage is very rapid. The usual criteria of large volume dosage effects cannot be applied where an intense dose is delivered to such a small volume of tissue.

One advantage as well as a limitation of the applicator is the highly localized radiation which it emits. It cannot affect excessive lymphoid tissue which is more than a few millimeters lateral to the pharyngeal orifice of the eustachian tube, and the exposure is limited even more unless midline adenoids have previously been surgically removed. Such highly localized radiation probably has little effect on the surrounding blood supply, although thickened, hyalinized arterioles and capillaries with prominent endothelial cells have been found in histologic sections of irradiated nasopharyngeal tissue (5). Because the volume irradiated is so small, much larger

exposures seem to be tolerated without significant reactions.

Satisfactory results are obtained from x-ray treatment of more diffuse lymphoid involvement of the naso-oro-pharynx with tissue doses of about 865 roentgens given in three weeks (600 r in air to each of two  $6 \times 8$ -cm. fields with a 10-cm. average width of skull) to a much greater volume of approximately 200 to 250 c.c. including Waldeyer's ring. This may be due to an anti-inflammatory effect rather than to one which depends upon any considerable destruction of lymphoid tissue for its results, although histologically many areas showed alteration of the germinal follicles, some of which consisted of only a few large reticulum cells. Normal, reactive, or non-neoplastic lymphoid tissue in general seems to resist destruction when given human therapeutic exposures, and even when it is adjacent to neoplasms which are heavily irradiated it is seldom completely eradicated, but it appears to be more sensitive in children. Beta radium therapy seems to be intended to relieve symptoms and not to attempt to remove all visible lymphoid tissue, and localized radiation with the applicator does not produce pharyngitis sicca, occasionally seen following x-ray treatment.

Since it has been determined clinically that these exposures are safe and are necessary to obtain the desired results, radiologists should apply this knowledge of accurate ionization measurements in using the applicator in the future.

HAROLD W. JACOX, M.D.

#### REFERENCES

1. BRAESTRUP, C. B.: Measurements of the Radiation Dose from the Nasopharyngeal Radium Beta-Gamma-Ray Applicator. *Tr. Am. Acad. Ophth.*, pp. 496-501, May-June 1950.
2. FOWLER, E. P., Jr.: Eustachian Tube Irradiation. *N. Y. State J. Med.* **49**: 187-190, Jan. 15, 1949.
3. PROCTOR, D. F., POLVOGT, L. M., AND CROWE, S. J.: Irradiation of Lymphoid Tissue in Diseases of the Upper Respiratory Tract. *Bull. Johns Hopkins Hosp.* **83**: 383-428, November 1948.
4. RUBIN, H. J., KULLY, B. M., AND FINKLE, R. D.: Radiation Exposure of Personnel Handling the Monel Metal Nasopharyngeal Radium Applicator. *Ann. Otol., Rhin. & Laryng.* **59**: 90-101, March 1950.
5. BILCHICK, E. B., AND KOLAR, A. R.: Radium Therapy for Lymphoid Tissue in the Nasopharynx. *Ann. Otol., Rhin. & Laryng.* **59**: 78-89, March 1950.

without

ed from  
ymphoid  
nx with  
s given  
a of two  
average  
olume of  
cluding  
e to an  
than to  
derable  
its re-  
y areas  
ollicles,  
a few  
eactive,  
in gen-  
n given  
d even  
ich are  
pletely  
e sensi-  
herapy  
ptoms  
nptoms  
visible  
diation  
roduce  
en fol-  
nically  
neces-  
radiolo-  
of ac-  
using  
M.D.

e Radia-  
n Beta-  
th., pp.

Irradia-  
5, 1949.  
CROWE,  
eases of  
Hopkins

R. D.:  
Monel  
Ann.

Radium  
harynx.  
950.

## RADIOLOGICAL SOCIETY OF NORTH AMERICA

### THIRTY-SIXTH ANNUAL MEETING

Chicago, Ill., Dec. 10-15, 1950

#### PRELIMINARY PROGRAM

Monday, December 11

OPENING SESSION: 10:30 A.M.

Call to Order. WARREN W. FUREY, M.D., President  
Address of Welcome. HARRY M. HEDGE, M.D., President,  
Illinois State Medical Society

#### Discussion of Medical Social Economic Problems

Presidential Address. WARREN W. FUREY, M.D.,  
Chicago, Ill.

Education. J. ROSCOE MILLER, M.D., President,  
Northwestern University, Evanston, Ill.

Can Voluntary Insurance Do the Job? LOWELL S.  
GOIN, M.D., President, California Medical Service,  
Los Angeles, Calif.

1:30-4:30 P.M.

Joseph C. Bell, M.D., Louisville, Ky., Presiding

The Use of Soft-Tissue Technic in the Diagnosis of  
Tumors of the Head and Neck. GILBERT H.  
FLETCHER, M.D., AND K. E. MATZINGER, M.D.  
(by invitation), Houston, Texas.

Cerebral Angiography in General Hospital Practice.  
HOWARD B. HUNT, M.D., AND RALPH C. MOORE,  
M.D., Omaha, Nebr.

Dural Sinus Venography. BRONSON S. RAY, M.D.,  
HOWARD S. DUNBAR, M.D., AND CHARLES T. DOT-  
TER, M.D., New York, N. Y. (by invitation).

John S. Bouslog, M.D., Denver, Colo., Presiding

Pituitary Irradiation in Prostatic Carcinoma. WALTER  
T. MURPHY, M.D., AND HARRY SCHWIPPERT, M.D.  
(by invitation), Buffalo, N. Y.

Physical and Clinical Aspects of Supervoltage Rota-  
tional Therapy. HUGH F. HARE, M.D., AND JOHN  
G. TRUMP, Ph.D. (by invitation), Boston, Mass.

Single Portal, Massive Dose, X-ray Therapy Technic  
for Treatment of Certain Cancers of the Mouth and  
Throat, Salivary Glands and Breast. MILTON  
FRIEDMAN, M.D., AND LAWRENCE DAVIS, M.D. (by  
invitation), New York, N. Y.

EXECUTIVE SESSION: 4:30 P.M.

Tuesday, December 12

10:30-12:00 Noon

Eugene P. Pendergrass, M.D., Philadelphia, Penna.,  
Presiding

Duodenal Ulcer in Children. FAY K. ALEXANDER,  
M.D., Germantown, Penna.

Enlarged Gastric Rugae: A Correlation of the Roent-  
genologic, Gastroscopic, Pathologic and Clinical  
Findings. WALTER W. VAUGHAN, M.D., Durham,  
N. C.

Steroids in Cancer of the Breast. RIEVA ROSH, M.D.,  
AND GEORGE G. GREEN, M.D. (by invitation), New  
York, N. Y.

Further Studies on the Radiosensitivity of Analogous  
Mammary Tumors in Inbred Strains of Animals.  
ANNA GOLDFEDER, D.Sc., M.U.C., New York, N. Y.

1:30-2:30 P.M.

Ira H. Lockwood, M.D., Kansas City, Mo., Presiding

History and Development of the Grid Technic in the  
Roentgen Treatment of Cancer. HIRSCH MARKS,  
M.D., New York, N. Y. (by invitation).

Depth Dose Curves for Grids in X-ray Therapy.  
ROBERT LOEVINGER, Ph.D., AND WALTER MINO-  
WITZ, B.E.E., New York, N. Y. (by invitation).

Recent Clinical Experience with the Grid in the X-ray  
Treatment of Advanced Cancer. WILLIAM HARRIS,  
M.D., New York, N. Y.

The Value of Cross Section Diagrams in Delivering  
Accurate X-ray Therapy into the Female Pelvis.  
JESSHILL LOVE, M. D., AND G. N. COMBS, M.D.,  
W. A. ASKEW, M.D., M. HARCOURT, A.B. (by invita-  
tion), Louisville, Ky.

EXECUTIVE SESSION AND INTERMISSION: 2:30 P.M.

3:30-4:30 P.M.

Thomas B. Bond, M.D., Ft. Worth, Texas, Presiding

Pulmonary Artery Thrombosis: Roentgen Manifesta-  
tions. JOSEPH HANELIN, M.D., AND WILLIAM R.  
EYLER, M.D., Boston, Mass. (by invitation).

Cardiac Mensuration as Applied to Survey Films.  
LEWIS G. JACOBS, M.D., AND HERMAN NUSSBAUM,  
M.D., Oakland, Calif.

Solitary Pulmonary Necrosis: A Comparison of Neoplastic and Inflammatory Conditions. RUSSELL WIGH, M.D., AND FREDERICK R. GILMORE, M.D., Philadelphia, Penna. (by invitation).

### THE CARMAN LECTURE: 8:00 P.M.

#### THE DEVELOPMENT OF CARDIOVASCULAR RADIOLOGY

Wendell G. Scott, M.D., St. Louis, Mo.

### Wednesday, December 13

#### CHICAGO DAY

10:30-12:00 Noon

Edward L. Jenkinson, M.D., Presiding

Round Table Discussion of Renal Tumors. VINCENT J. O'CONOR, M.D., J. KENNETH SOKOL, M.D., THOMAS C. LAIPPLY, M.D. (by invitation), AND EARL E. BARTH, M.D., AND ABRAM H. CANNON, M.D., Northwestern University Medical School.

The End Results in Ovarian Cancer Treated by Surgery and Irradiation. HERBERT E. SCHMITZ, M.D., AND JOSEPH T. MAJEWSKI, M.D. (by invitation).

Indications for Surgery in Carcinoma of the Cervix. JANET E. TOWNE, M.D., AND CHARLES J. SMITH, M.D., Stritch School of Medicine of Loyola University (by invitation).

1:30-3:00 P.M.

Benjamin H. Orndoff, M.D., Presiding

Multiple and Solitary Infarctions of Bone. DALLAS B. PHEMISTER, M.D. (by invitation).

The Reaction of the Alimentary Tract to ACTH. WALTER L. PALMER, M.D., AND JOSEPH B. KIRSNER, M.D. (by invitation).

Pelvic Dimensions in Eutocia and Dystocia. PAUL C. HODGES, M.D., AND RUSSELL L. NICHOLS, M.D., University of Chicago, Department of Medicine.

Radiation Therapy of Malignant Melanoma. PAUL H. REITMAN, M.D.

Evaluation of Results in Patients with Breast Cancer Who Routinely Received Radiation. ERICH H. UHLMANN, M.D., Michael Reese Hospital.

### INTERMISSION 3:00-3:30 P.M.

3:30-4:30 P.M.

Robert A. Arens, M.D., Presiding

Correlation and Evaluation of Postmortem Pathology with X-rays of the Chest. DAVID S. BEILIN, M.D., AND JACK P. FINK, M.D., AND LAWRENCE W. LESLIE, M.D. (by invitation), Augustana Hospital.

Symposium on Diagnosis of Primary Lung Neoplasm. PAUL H. HOLINGER, M.D., AND WILLARD VAN HAZEL, M.D. (by invitation), AND THEODORE J. WACHOWSKI, M.D., University of Illinois College of Medicine.

### Thursday, December 14

10:30-12:00 Noon

Leo G. Rigler, M.D., Minneapolis, Minn., Presiding

Intensification of the Fluorescent Screen: The Practicability of Electronic Systems of the Storage Type. RUSSELL H. MORGAN, M.D., AND RALPH E. STURM (by invitation), Baltimore, Md.

Reticulo-Endotheliosis (Hand-Schüller-Christian Disease). JOHN R. HODGSON, M.D., R. L. J. KENNEDY, M.D. (by invitation), AND JOHN D. CAMP, M.D., Rochester, Minn.

The Treatment of Reticulo-Endotheliosis with Roentgen Rays. DONALD S. CHILDS, JR., M.D. Rochester, Minn.

The Co<sup>60</sup> Nylon Threads, a New Interstitial Radiation Therapy. JOSEPH L. MORTON, M.D., GEORGE W. CALLENDINE, M.S., AND WILLIAM G. MYERS, Ph.D., M.D., Columbus, Ohio (by invitation).

1:30-2:30 P.M.

Sydney J. Hawley, M.D., Seattle, Wash., Presiding

Radioactive Iodine in Medicine. EARL R. MILLER, M.D., San Francisco, Calif.

Treatment of Intractable Heart Disease with Radioactive Iodine (I<sup>131</sup>). RICHARD H. CHAMBERLAIN, M.D., AND CHARLES C. WOLFERTH, M.D., JACK EDEKEN, M.D., JOHN J. MEAD, M.D. (by invitation), Philadelphia, Penna.

The Scintillation Counter in Clinical Studies of Human Thyroid Physiology Using I<sup>131</sup>. HERBERT C. ALLEN, JR., M.D., RAYMOND L. LIBBY, Ph.D., AND BENEDICT CASSEN, Ph.D., Los Angeles, Calif. (by invitation).

### EXECUTIVE SESSION AND INTERMISSION: 2:30 P.M.

3:30-4:30 P.M.

Edward B. D. Neuhauser, M.D., Boston, Mass., Presiding

Diagnostic Studies with Radioactive Isotope Tracers. LAWRENCE REYNOLDS, M.D., HENRIETTA S. HAYDEN, Ph.D., AND KENNETH E. CORRIGAN, Ph.D., Detroit, Mich.

Hepatolienography: Past, Present and Future. GEORGE HENRY, M.D. (by invitation), AND SYDNEY F. THOMAS, M.D., Palo Alto, Calif.

Roentgen Demonstration of the Venous Circulation in the Liver: Portal Venography. GEORGE E. MOORE, M.D., AND RICHARD B. BRIDENBAUGH, M.D., Minneapolis, Minn. (by invitation).

## ANNUAL BANQUET: 7:00 P.M.

Friday, December 15

10:30-12:00 Noon

John H. Gilmore, M.D., Chicago, Ill., Presiding

Pulmonary Complications of Acute Bulbar Poliomyelitis. GEORGE JACOBSON, M.D., RAY A. CARTER, M.D., AND SEYMOUR R. COHEN, M.D. (by invitation), Los Angeles, Calif.

Iodinated Organic Compounds as Contrast Media for Radiographic Diagnosis. XII. Studies on the Physiology of Cholecystography. ROBERT H. GREENLAW, B.S., MICHAEL RODAKOVICH, M.D., HAROLD D. ROBERTSON, M.D., WILLIAM H. STRAIN, Ph.D., JAMES M. DENNIS, GEORGE H. RAMSEY,

M.D., AND CHARLES E. SHERWOOD, M.D., Rochester, N. Y. (by invitation).

Plasma Proteins in Cancer. CHARLES B. HUGGINS, M.D., AND E. V. JENSEN, M.D., Chicago, Ill. (by invitation).

Frank L. Hussey, M.D., Chicago, Ill., Presiding

Nitrogen Mustard as an Adjunct to Radiation in the Management of Bronchogenic Cancer. BERNARD ROSWIT, M.D., AND GUSTAVE KAPLAN, M.D. (by invitation), New York, N. Y.

Diagnosis of Intrathoracic Lymph Node Metastases in Carcinoma of the Lung. JAMES J. MCCORT, M.D., AND LAURENCE L. ROBBINS, M.D., Boston, Mass.

Betatron Cancer Therapy. ROGER A. HARVEY, M.D., AND LEWIS L. HAAS, M.D., AND JOHN S. LAUGHLIN, Ph.D. (by invitation), Chicago, Ill.



## ANNOUNCEMENTS AND BOOK REVIEWS

### NEW ENGLAND ROENTGEN RAY SOCIETY

The newly elected officers of the New England Roentgen Ray Society are: President, Dr. George Levene; Vice-President, Dr. Jack Spencer; Treasurer, Dr. Joseph H. Marks; Secretary, Dr. L. L. Robbins, Massachusetts General Hospital, Boston.

### RADIOLOGICAL SOCIETY OF NEW JERSEY

At the annual meeting of the Radiological Society of New Jersey, held on May 22, in Atlantic City, the following officers were elected: President, Dr. Raphael Pomeranz, of Newark; Vice-President, Dr. Benjamin Copleman, of Perth Amboy; Treasurer, Dr. V. M. Whelan, of Red Bank; Secretary, Dr. Peter J. Gianquinto, 685 High St., Newark 2.

### SYMPOSIUM ON ISOTOPES

The New York Section of the American Chemical Society has scheduled an all-day "Symposium on Radioisotopes" to be held in the Hotel Statler, New York City, Friday, January 19, 1951. The first session will convene at 2:00 P.M., and the second at 7:30 P.M. Dr. Paul C. Aebersold, Chief of the Isotopes Division, U. S. Atomic Energy Commission, will preside. The complete program will be published at a later date.

### ERRATUM

In the drawing at the foot of page 841 (Fig. 10) in the paper on Roentgen Treatment of Cancer of the Cervix, by Gilbert H. Fletcher, M.D., in the June 1950 issue of *RADIOLOGY*, the last two lines in the first column, showing dosage, should read as follows:

Mx. T.D.  $2400 \times 1.4 = 3360$  r

Mn. T.D.  $2400 \times 1.2 = 2880$  r

### Books Received

Books received are acknowledged under this heading, and such notice may be regarded as recognition of the courtesy of the sender. Reviews will be published in the interest of our readers and as space permits.

**THE ESOPHAGUS AND PHARYNX IN ACTION. A STUDY OF STRUCTURE IN RELATION TO FUNCTION.** By WILLIAM LERCHE, M.D., Fellow, American College of Surgeons; Founder Member and Honorary Member of the American Association for Thoracic Surgery; Formerly, Associate Professor of Surgery, University of Minnesota, Minneapolis, Minn. A volume of 230 pages, with 105 illustrations. Published by Charles C Thomas, Springfield, Ill., 1950. Price \$5.50.

**THE CLINICAL USE OF RADIOACTIVE ISOTOPES.** By BERTRAM V. A. LOW-BEER, M.D., Associate Professor of Radiology, University of California Medical School, San Francisco, Calif. Publication No. 54, American Lecture Series, a monograph in American Lectures in Radiation Therapy, edited by Milton R. Friedman, M.D. A volume of 436 pages, with 105 illustrations. Published by Charles C Thomas, Springfield, Ill., 1950. Price \$9.50.

**POST-GRADUATE LECTURES ON ORTHOPEDIC DIAGNOSIS AND INDICATIONS.** By ARTHUR STEINDLER, M.D., F.A.C.S., Professor of Orthopedic Surgery, State University of Iowa, Iowa City, Iowa. Volume I, Section A: Propedeutics in Orthopedic Diagnosis; Section B: Congenital Deformities and Disabilities. A volume of 302 pages, with 400 illustrations. Published by Charles C Thomas, Springfield, Ill., 1950. Price \$7.50.

**RESEARCHES ON THE RADIOTHERAPY OF ORAL CANCER.** By CONSTANCE A. P. WOOD and J. W. BOAG (with P. HOWARD-FLANDERS, A. GLÜCKSMANN, L. H. GRAY, and F. G. SPEAR). Medical Research Council Special Report Series No. 267. A monograph of 148 pages, with 77 illustrations and 31 tables. Published by His Majesty's Stationery Office, 429 Oxford St., London, W. I., 1950. May be obtained through the British Information Services, 30 Rockefeller Plaza, New York 20, N. Y. Price 12s. 6d. Net.

**SOME APPLICATIONS OF NUCLEAR PHYSICS TO MEDICINE.** Supplement No. 2, British Journal of Radiology. By W. V. MAYNEORD, D.Sc., F. Inst. P., Professor of Physics applied to Medicine, University of London; Physicist to the Royal Cancer Hospital. Hon. Editor, C. W. Wilson. A monograph of 290 pages, with 152 illustrations and 43 tables. Published by the British Institute of Radiology, London, 1950. Price 35s.

**STUDIES ON THE CLASSIFICATION OF CARCINOMA OF THE UTERUS. A PATHO-ANATOMICAL AND CLINICAL INVESTIGATION.** Acta Radiologica Supplement 78. By HERMAN LEISSNER. From the Department of Gynaecology (Chief, at the time in question: Professor J. Heyman) and the Department of Radiopathology (Chief: Professor O. Reuterwall) of the Radiumhemmet, Stockholm, Sweden. A monograph of 106 pages, with numerous diagrams illustrating the cases reported. Elanders Boktryckeri Aktiebolag, Göteborg, Sweden, 1950.

**HYSTEROGRAPHY IN CANCER OF THE CORPUS OF THE UTERUS.** Acta Radiologica Supplement 79. By OLOF NORMAN. From the Roentgen-Diagnostic Department of the University Clinics of Lund (Head: Professor Olle Olsson), the Gynecological Department of King Gustaf V's Jubilee Clinic in Lund (Head: Doctor Gunnar Gorton), and the Obstetrical and Gynecological Clinic of the University of Lund (Head: Professor Alf Sjövall). A monograph of 156 pages, with 57 figures and diagrams illustrating 128 cases. Berlingska Boktryckeriet, Lund, Sweden, 1950.

**ODONTOGENIC CYSTS AND CYSTIC TUMOURS OF THE JAWS.** A ROENTGEN-DIAGNOSTIC AND PATHO-ANATOMIC STUDY. Acta Radiologica Supplement 81. By ANDERS SONESSON. From the Roentgen-Diagnostic Department of the University Clinics of Lund, Sweden (Head: Professor Olle Olsson, M.D.). A monograph of 160 pages, with 121 illustrations. Berlingska Boktryckeriet, Lund, Sweden, 1950.

**HEART VOLUME IN NORMAL INFANTS.** A ROENTGENOLOGICAL STUDY. Acta Radiologica Supplement 82. By JOHN LIND. From the Paediatric Clinic of Karolinska Institutet, at the Norrtull's Hospital, Stockholm, Sweden. Head: Professor Arvid Wallgren. A monograph of 128 pages with 24 charts and 11 tables. Alb. Bonniers Boktryckeri, Stockholm, 1950.

**UNFALLCHIRURGIE IM RÖNTGENBILDE.** By DR. WALTHER EHALT, Leiter des Unfallkrankenhauses in Graz, with foreword by PROFESSOR DR. LORENZ BÖHLER, Wien, Leiter des Unfallkrankenhauses in Wien. A volume of 620 pages, with 1,379 illustrations and 14 tables. Verlag Wilhelm Maudrich, Wien, 1950.

**LE ZONE POLMONARI.** By DR. LUCIO DI GUGLIELMO. From Istituto di Radiologia e Terapia Fisica dell'Università di Pavia (Direttore: Prof. A. Ratti) and Istituto di Radiologia e Terapia Fisica dell'Università di Napoli (Direttore inc.: Prof. G. Muscettola). Preface by PROFESSOR ARDUINO RATTI. A volume of 304 pages, with 231 illustrations and 4 color plates. Edizioni Scientifiche Italiane, Naples, 1949.

## Book Reviews

**LA RADIODIAGNOSTICA DEI TUMORI CEREBRALI.** By PROF. FERMO MASCHERPA. Vol. I, Part I. Atti del XVI Congresso nazionale di radiologia medica, Taormina, 15-18 May 1950. A monograph of 126 pages, with 124 illustrations. Tipografia Ditta D'Amico, Messina, 1950.

This monograph represents a summary of the large experience of the author during his service at

the Neurological Institute at the University of Milan. In the first part of the book Professor Mascherpa discusses the various methods of examination, beginning with the simple radiograph of the skull and following through with encephalography, fractional encephalography, cisternography, ventriculography, arteriography and the use of opaque materials for visualization of the aqueduct of Sylvius. These various methods are considered in detail and the indications for each are thoroughly shown. A great deal of stress is placed on the combination of the various methods of examination, and many beautiful illustrations show how patients were studied by the successive use of two or more methods before a positive diagnosis could be made.

The second part of the book deals with the special radiological symptomatology of the various cerebral lesions and tumors, considering them according to their nature and localization. This monograph is very well written, the illustrations are excellent, and the author shows a thorough knowledge of the subject.

**LA RADIOTERAPIA DEI TUMORI MALIGNI DEL SISTEMA RETICOLOENDOTELIALE.** By PROF. GIOVANNI F. GARDINI. Vol. I, Part II. Atti del XVI Congresso nazionale di radiologia medica, Taormina, 15-18 May, 1950. A monograph of 78 pages. Tipografia Ditta D'Amico, Messina, 1950.

The author reports on the tumors of the reticulo-endothelial system observed at the Radium Institute directed by Prof. Palmieri. There were twenty-three cases of glandular localization, seven cases of subcutaneous tumors, four cases in which the tumors were found in the nasopharynx, three cases of bone tumors, two cases of tumors of the hard palate and one each of the testicle, vagina, thyroid, and gums. Best results were obtained in the localized forms of the glandular type and in lesions localized to the nasopharynx, to the tonsils, and to the subcutaneous tissue.

The author admits quite frankly that a great deal of confusion exists among the pathologists as to the exact nature and classification of these tumors. This makes it difficult to predict the radiotherapeutic response of a certain tumor even when the histologic appearance seems to be fairly typical. It is obvious that the name "reticulo-endothelial tumors" is still somewhat of a dumping ground for pathologists. This unfortunate fact greatly impairs the value of otherwise careful radiological work.

**RADIOTERAPIA E RADIOBIOLOGIA DEI TUMORI DELLE OSSA.** By PROF. ADAMO GRILLI. Vol. I, Part III. Atti del XVI Congresso nazionale di radiologia medica, Taormina 15-18 May, 1950. A monograph of 202 pages, with 57 illustrations. Abruzzini Editore, Rome 1950.

This monograph on bone tumors is a valuable attempt to give the radiologist a digested account of

the present knowledge of this subject. The author has collected a large amount of material at the Institute of Radiology at the University of Rome and has studied and assimilated the fundamental works which have appeared in this field, combining the published information with his own knowledge and experience. In the first two chapters of his book, Professor Grilli discusses the statistical incidence and localization of bone tumors. Considerable space is devoted to discussion of the various classifications proposed up to now. The third and fourth chapters include descriptions of the sensitivity of the various types of bony neoplasms to radiation and radioisotopes.

In the second part of his book, the author discusses in detail the technic of irradiation and the results obtained in his cases of osteogenic sarcoma, reticulo-endothelial sarcomas, myelomas, giant-cell tumors, tumors originating from cartilaginous inclusions, and skeletal metastases. The book is well printed and beautifully illustrated and should prove to be a handy reference manual for those interested in tumors of the bone.

### In Memoriam

PRESSLEY A. KIBBE, M.D.

Pressley Aloysius Kibbe, head of the Department of Radiology at Hôtel Dieu, New Orleans, La., since 1945, died at that hospital on Friday, Aug. 4, following a hospitalization of two weeks.

Born in January 1891 in Vermillion Parish, Louisiana, Dr. Kibbe was graduated from the Tulane University School of Medicine in 1912. Following an internship, he entered general practice in his home town of Erath, La. During World War I, he served as a captain in the Army Medical Corps until he was retired for reasons of health.

Dr. Kibbe came to Hôtel Dieu as an anesthetist in



Pressley A. Kibbe, M.D.

1924 but gradually became more interested in radiology. In 1930 he became associated with Drs. Lucien A. Fortier and Tracy T. Gatley in the Department of Radiology, serving as an associate until he was named head of the department in 1945. He served in this capacity until his death.

Dr. Kibbe was certified by the American Board of Radiology in 1941. He was a member of the American College of Radiology, the Radiological Society of North America, and the Louisiana State and Orleans Parish Medical Societies.

Although he suffered from a severe coronary impairment from his early twenties, Dr. Kibbe did not spare himself. It was not until the last year of his life that he curtailed his activities because of his failing health. He was known to his colleagues as a tireless worker during the years he served Hôtel Dieu, and his services as a diagnostician were highly valued.

Dr. Kibbe is survived by one son, three daughters, and two brothers.

HENRY DUHE, M.D.



## RADIOLOGICAL SOCIETIES: SECRETARIES AND MEETING DATES

*Editor's Note:* Secretaries of state and local radiological societies are requested to co-operate in keeping this section up-to-date by notifying the editor promptly of changes in officers and meeting dates.

**RADIOLOGICAL SOCIETY OF NORTH AMERICA.** *Secretary-Treasurer*, Donald S. Childs, M.D., 713 E. Genesee St., Syracuse 2, N. Y.

**AMERICAN RADIUM SOCIETY.** *Secretary*, John E. Wirth, M.D., Baltimore, Md.

**AMERICAN ROENTGEN RAY SOCIETY.** *Secretary*, Barton R. Young, M.D., Germantown Hospital, Philadelphia 44, Penna.

**AMERICAN COLLEGE OF RADIOLOGY.** *Secretary*, William C. Stronach, 20 N. Wacker Dr., Chicago 6, Ill.

**SECTION ON RADIOLOGY, A. M. A.** *Secretary*, Paul C. Hodges, M.D., 950 East 59th St., Chicago 37.

### Alabama

**ALABAMA RADIOLOGICAL SOCIETY.** *Secretary-Treasurer*, W. D. Anderson, M.D., 420 10th St., Tuscaloosa.

### Arizona

**ARIZONA ASSOCIATION OF PATHOLOGISTS AND RADIOLOGISTS.** *Secretary*, R. Lee Foster, M.D., 507 Professional Bldg., Phoenix.

### Arkansas

**ARKANSAS RADIOLOGICAL SOCIETY.** *Secretary*, Fred Hames, M.D., Pine Bluff. Meets every three months and at meeting of State Medical Society.

### California

**CALIFORNIA MEDICAL ASSOCIATION, SECTION ON RADIOLOGY.** *Secretary*, Sydney F. Thomas, M.D., Palo Alto Clinic, Palo Alto.

**EAST BAY ROENTGEN SOCIETY.** *Secretary*, Dan Tucker, M.D., 434 30th St., Oakland 9. Meets monthly, first Thursday, at Peralta Hospital.

**LOS ANGELES RADIOLOGICAL SOCIETY.** *Secretary*, Harold P. Tompkins, M.D., 658 South Westlake Ave. Meets monthly, second Wednesday, County Society Bldg.

**NORTHERN CALIFORNIA RADIOLOGICAL CLUB.** *Secretary*, Clifford W. Wauters, 701 High St., Auburn. Meets at dinner last Monday of September, November, January, March, and May.

**PACIFIC ROENTGEN SOCIETY.** *Secretary*, L. Henry Garland, M.D., 450 Sutter St., San Francisco 8. Meets annually with State Medical Association.

**SAN DIEGO ROENTGEN SOCIETY.** *Secretary*, R. F. Niehaus, M.D., 1831 Fourth Ave., San Diego. Meets first Wednesday of each month.

**X-RAY STUDY CLUB OF SAN FRANCISCO.** *Secretary*, Merrell A. Sisson, M.D., 450 Sutter St., San Francisco 8. Meets third Thursday at 7:45, January to June at Stanford University Hospital, July to December at San Francisco Hospital.

### Colorado

**COLORADO RADIOLOGICAL SOCIETY.** *Secretary*, Paul E. RePass, M.D., 306 Republic Bldg., Denver 2. Meets monthly, third Friday, at University of Colorado Medical Center or Denver Athletic Club.

### Connecticut

**CONNECTICUT STATE MEDICAL SOCIETY, SECTION ON RADIOLOGY.** *Secretary*, Fred Zaff, M.D., 135 Whitney Ave., New Haven. Meetings bimonthly, second Wednesday.

**CONNECTICUT VALLEY RADIOLOGICAL SOCIETY.** *Secretary*, Ellwood W. Godfrey, M.D., 1676 Boulevard, W. Hartford. Meets second Friday of October and April.

### District of Columbia

**RADIOLOGICAL SECTION, DISTRICT OF COLUMBIA MEDICAL SOCIETY.** *Secretary*, Karl C. Corley, M.D., 1835 Eye St., N.W., Washington 6. Meets third Thursday, January, March, May, and October, at 8:00 P.M., in Medical Society Auditorium.

### Florida

**FLORIDA RADIOLOGICAL SOCIETY.** *Secretary-Treasurer*, John J. McGuire, M.D., 1117 N. Palafox, Pensacola. Meets in April and in November.

**GREATER MIAMI RADIOLOGICAL SOCIETY.** *Secretary*, David Kirsh, M.D., 712 duPont Bldg., Miami 32. Meets monthly, last Wednesday, 8:00 P.M.

### Georgia

**ATLANTA RADIOLOGICAL SOCIETY.** *Secretary-Treasurer*, Ted F. Leigh, M.D., Emory University Hospital. Meets second Friday, September to May.

**GEORGIA RADIOLOGICAL SOCIETY.** *Secretary-Treasurer*, Robert C. Pendergrass, M.D., Americus. Meets in November and at the annual meeting of State Medical Association.

### Illinois

**CHICAGO ROENTGEN SOCIETY.** *Secretary*, Benjamin D. Brauh, M.D., 6 N. Michigan Ave., Chicago 11. Meets at the University Club, second Thursday of October, November, January, February, March, and April at 8:00 P.M.

**ILLINOIS RADIOLOGICAL SOCIETY.** *Secretary-Treasurer*, William DeHollander, M.D., St. Johns' Hospital, Springfield. Meetings quarterly as announced.

**ILLINOIS STATE MEDICAL SOCIETY, SECTION ON RADIOLOGY.** *Secretary*, Willard C. Smullen, M.D., St. Mary's Hospital, Decatur.

### Indiana

**INDIANA ROENTGEN SOCIETY.** *Secretary-Treasurer*, William M. Loehr, M.D., 712 Hume-Mansur Bldg., Indianapolis 4. Annual meeting in May.

### Iowa

**IOWA X-RAY CLUB.** *Secretary*, Arthur W. Erskine, M.D., 326 Higley Building, Cedar Rapids. Meets during annual session of State Medical Society.

**Kansas**

KANSAS RADIOLOGICAL SOCIETY. *Secretary*, Anthony F. Rossitto, M.D., Wichita Hospital, Wichita. Meets annually with State Medical Society.

**Kentucky**

LOUISVILLE RADIOLOGICAL SOCIETY. *Secretary*, Everett L. Pirkey, M.D., Louisville General Hospital. Meets monthly, second Friday, at Seelbach Hotel.

**Louisiana**

LOUISIANA RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Johnson R. Anderson, M.D., No. Louisiana Sanitarium, Shreveport. Meets with State Medical Society.

ORLEANS PARISH RADIOLOGICAL SOCIETY. *Secretary*, Joseph V. Schlosser, M.D., Charity Hospital of Louisiana, New Orleans 13. Meets first Tuesday of each month.

SHREVEPORT RADIOLOGICAL CLUB. *Secretary*, Oscar O. Jones, M.D., 2622 Greenwood Road. Meets monthly September to May, third Wednesday.

**Maine**

MAINE RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Clark F. Miller, M.D., Central Maine General Hospital, Lewiston.

**Maryland**

BALTIMORE CITY MEDICAL SOCIETY, RADIOLOGICAL SECTION. *Secretary*, J. Howard Franz, M.D., 1127 St. Paul St., Baltimore 2.

**Michigan**

DETROIT X-RAY AND RADIUM SOCIETY. *Secretary*, James C. Cook, M.D., Harper Hospital, Detroit 1. Meetings first Thursday, October to May, at Wayne County Medical Society club rooms.

MICHIGAN ASSOCIATION OF ROENTGENOLOGISTS. *Secretary-Treasurer*, R. B. MacDuff, M.D., 220 Genesee Bank Building, Flint 3.

**Minnesota**

MINNESOTA RADIOLOGICAL SOCIETY. *Secretary*, Leo A. Nash, M.D., 572 Lowry Medical Arts Bldg., St. Paul 2. Meets in Spring and Fall.

**Missouri**

RADIOLOGICAL SOCIETY OF GREATER KANSAS CITY. *Secretary*, Wm. M. Kitchen, M.D., 1010 Rialto Building, Kansas City 6, Mo. Meetings last Friday of each month.

ST. LOUIS SOCIETY OF RADIOLOGISTS. *Secretary*, H. R. Senturia, M.D., Pasteur Medical Bldg. Meets on fourth Wednesday, October to May.

**Nebraska**

NEBRASKA RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, John E. Downing, M.D., 816 Medical Arts Bldg., Omaha. Meets fourth Thursday of each month at 6 P.M. in Omaha or Lincoln.

**New England**

NEW ENGLAND ROENTGEN RAY SOCIETY. *Secretary*, L. L. Robbins, M.D., Massachusetts General Hospital, Boston 14. Meets monthly on third Friday at the Harvard Club.

**New Hampshire**

NEW HAMPSHIRE ROENTGEN SOCIETY. *Secretary*, Albert C. Johnston, M.D., Elliot Community Hospital, Keene. Meetings quarterly in Concord.

**New Jersey**

RADIOLOGICAL SOCIETY OF NEW JERSEY. *Secretary*, Peter J. Gianquinto, M.D., 685 High St., Newark 2. Meets at Atlantic City at time of State Medical Society and midwinter in Elizabeth.

**New York**

ASSOCIATED RADIOLOGISTS OF NEW YORK, INC. *Secretary*, William J. Francis, M.D., East Rockaway.

BROOKLYN ROENTGEN RAY SOCIETY. *Secretary*, J. Daversa, M.D., 603 Fourth Ave., Brooklyn. Meets fourth Tuesday, October to April.

BUFFALO RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Mario C. Gian, M.D., 610 Niagara St., Buffalo 1. Meetings second Monday, October to May.

CENTRAL NEW YORK ROENTGEN SOCIETY. *Secretary*, Dwight V. Needham, M.D., 608 E. Genesee St., Syracuse 10. Meetings January, May, October.

KINGS COUNTY RADIOLOGICAL SOCIETY. *Secretary*, Marcus Wiener, M.D., 1430 48th St., Brooklyn 19. Meetings fourth Thursday evening, October to May, at 8:45 P.M., in Kings County Medical Bldg.

NEW YORK ROENTGEN SOCIETY. *Secretary*, John L. Olpp, M.D., 49 Ivy Lane, Tenafly, N. J.

QUEENS ROENTGEN RAY SOCIETY. *Secretary*, Jacob E. Goldstein, M.D., 88-29 163rd St., Jamaica 3. Meets fourth Monday of each month.

ROCHESTER ROENTGEN-RAY SOCIETY. *Secretary-Treasurer*, A. Vaughn Winchell, M.D., 40 Meigs St. Meets at Strong Memorial Hospital, last Monday of each month, September through May.

**North Carolina**

RADIOLOGICAL SOCIETY OF NORTH CAROLINA. *Secretary*, James E. Hemphill, M.D., Professional Bldg., Charlotte 2. Meets in May and October.

**North Dakota**

NORTH DAKOTA RADIOLOGICAL SOCIETY. *Secretary*, Charles Heilman, M.D., 807 Broadway, Fargo.

**Ohio**

OHIO STATE RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Edward C. Elsey, M.D., 927 Carew Tower, Cincinnati 2. Meets with State Medical Association.

CENTRAL OHIO RADIOLOGICAL SOCIETY. *Secretary*, Frank A. Riebel, M.D., 15 W. Goodale St., Columbus. Meets second Thursday, October, December, February, April, and June, 6:30 P.M., Columbus Athletic Club, Columbus.

CINCINNATI RADIOLOGICAL SOCIETY. *Secretary*, Edward C. Elsey, M.D. Meets last Monday, September to May.

CLEVELAND RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, John R. Hannan, M.D., 10515 Carnegie Ave., Cleveland 6. Meetings at 6:45 P.M. on fourth Monday, October to April, inclusive.

**MIAMI VALLEY RADIOLOGICAL SOCIETY.** *Secretary,* Geo. A. Nicoll, M.D., Miami Valley Hospital, Dayton. Meets monthly, second Friday.

#### Oklahoma

**OKLAHOMA STATE RADIOLOGICAL SOCIETY.** *Secretary-Treasurer,* W. E. Brown, M.D., 21st and Xanthus, Tulsa 4. Meets in October, January, and May.

#### Oregon

**OREGON RADIOLOGICAL SOCIETY.** *Secretary-Treasurer,* C. Todd Jessell, M.D., 224 Medical-Dental Bldg., Portland 5. Meets monthly, on the second Wednesday, at 8:00 P.M., in the library of the University of Oregon Medical School.

#### Pacific Northwest

**PACIFIC NORTHWEST RADIOLOGICAL SOCIETY.** *Secretary-Treasurer,* Sydney J. Hawley, M.D., 1320 Madison St., Seattle 4. Meets annually in May.

#### Pennsylvania

**PENNSYLVANIA RADIOLOGICAL SOCIETY.** *Secretary-Treasurer,* James M. Converse, M.D., 416 Pine St., Williamsport 8. Meets annually.

**PHILADELPHIA ROENTGEN RAY SOCIETY.** *Secretary,* George P. Keefer, M.D., American Oncologic Hospital, Philadelphia 4. Meets first Thursday of each month at 8:00 P.M., from October to May, in Thomson Hall, College of Physicians, 21 S. 22nd St.

**PITTSBURGH ROENTGEN SOCIETY.** *Secretary-Treasurer,* Edwin J. Euphrat, M.D., 3500 Fifth Ave., Pittsburgh 13. Meets monthly, second Wednesday, at 6:30 P.M., October to May, at Webster Hall.

#### Rocky Mountain States

**ROCKY MOUNTAIN RADIOLOGICAL SOCIETY.** *Secretary-Treasurer,* Maurice D. Frazer, M.D., Lincoln Clinic, Lincoln, Nebr.

#### South Carolina

**SOUTH CAROLINA X-RAY SOCIETY.** *Secretary-Treasurer,* S. H. Fisher, M.D., 107 E. North St., Greenville. Meets with State Medical Association in May.

#### South Dakota

**RADIOLOGICAL SOCIETY OF SOUTH DAKOTA.** *Secretary-Treasurer,* Marianne Wallis, M.D., 1200 E. Fifth Ave., Mitchell. Meets with State Medical Society.

#### Tennessee

**MEMPHIS ROENTGEN CLUB.** Meetings second Tuesday of each month at University Center.

**TENNESSEE RADIOLOGICAL SOCIETY.** *Secretary-Treasurer,* J. Marsh Frère, M.D., 707 Walnut St., Chattanooga. Meets annually with State Medical Society in April.

#### Texas

**DALLAS-FORT WORTH ROENTGEN STUDY CLUB.** *Secretary,* X. R. Hyde, M.D., Medical Arts Bldg., Fort Worth 2. Meets monthly, third Monday, in Dallas odd months, Fort Worth even months.

**HOUSTON X-RAY CLUB.** *Secretary,* Curtis H. Burge, M.D., 3020 San Jacinto, Houston 4. Meetings fourth Monday of each month.

**TEXAS RADIOLOGICAL SOCIETY.** *Secretary-Treasurer,* R. P. O'Bannon, M.D., 650 Fifth Ave., Fort Worth. Next meeting, Jan. 19-20, 1951, in Galveston.

#### Utah

**UTAH STATE RADIOLOGICAL SOCIETY.** *Secretary-Treasurer,* Angus K. Wilson, M.D., 343 S. Main St., Salt Lake City. Meets third Wednesday, January, March, May, September, November.

#### Virginia

**VIRGINIA RADIOLOGICAL SOCIETY.** *Secretary,* P. B. Parsons, M.D., Norfolk General Hospital, Norfolk.

#### Washington

**WASHINGTON STATE RADIOLOGICAL SOCIETY.** *Secretary-Treasurer,* R. C. Kiltz, M.D., 705 Medical-Dental Bldg., Everett. Meetings fourth Monday, October through May, at College Club, Seattle.

#### Wisconsin

**MILWAUKEE ROENTGEN RAY SOCIETY.** *Secretary-Treasurer,* Theodore J. Pfeffer, M.D., 839 N. Marshall St., Milwaukee 2. Meets monthly on second Monday at the University Club.

**RADIOLOGICAL SECTION OF THE WISCONSIN STATE MEDICAL SOCIETY.** *Secretary,* Abraham Melamed, M.D., 425 E. Wisconsin Ave., Milwaukee. Meets in May and with State Medical Society, September.

**UNIVERSITY OF WISCONSIN RADIOLOGICAL CONFERENCE.** Meets first and third Thursdays 4 P.M., September to May, Service Memorial Institute, Madison 6.

**WISCONSIN RADIOLOGICAL SOCIETY.** *Secretary-Treasurer,* Irving I. Cowan, M.D., 425 East Wisconsin Ave., Milwaukee 2.

#### Puerto Rico

**ASOCIACIÓN PUERTORRIQUEÑA DE RADIOLOGÍA.** *Secretary,* Jesús Rivera Otero, M.D., Box 3542, San-turce, Puerto Rico.

#### CANADA

**CANADIAN ASSOCIATION OF RADIOLOGISTS.** *Honorary Secretary-Treasurer,* Jean Bouchard, M.D. *Associate Honorary Secretary-Treasurer,* D. L. McRae, M.D. *Central Office,* 1555 Summerhill Ave., Montreal 26, Quebec. Meetings in January and June.

**LA SOCIÉTÉ CANADIENNE-FRANÇAISE D'ELECTROLOGIE ET DE RADIOLOGIE MÉDICALES.** *General Secretary,* Origène Dufresne, M.D., Institut du Radium, Montreal. Meets third Saturday each month.

#### CUBA

**SOCIEDAD DE RADIOLOGÍA Y FISIOTERAPIA DE CUBA.** Offices in Hospital Mercedes, Havana. Meets monthly.

#### MEXICO

**SOCIEDAD MEXICANA DE RADIOLOGÍA Y FISIOTERAPIA.** *General Secretary,* Dr. Dionisio Pérez Cosío, Marsella 11, México, D. F. Meetings first Monday of each month.

#### PANAMA

**SOCIEDAD RADIOLÓGICA PANAMEÑA.** *Secretary-Editor,* Luis Arrieta Sánchez, M.D., Apartado No. 86, Panama, R. de P.

## ABSTRACTS OF CURRENT LITERATURE

### ROENTGEN DIAGNOSIS

#### The Head and Neck

- BULL, JAMES W. D. A Review of Cerebral Angiography..... 607
- PENNYBACKER, JOE. Intracranial Tumours in the Aged..... 607
- WALKER, A. EARL, AND HOPPLE, THERON L. Brain Tumors in Children..... 608
- NORDMARK, BENGT. Pressure Changes in the Sella Turcica in the Presence of Glioma in the Cerebral Hemispheres..... 608
- ELVIDGE, ARTHUR R., AND JACKSON, IRA J. Subdural Hematoma and Effusion in Infants.... 608
- FLEISCHNER, FELIX G., AND SHALEK, SEYMOUR R. Conjunctival and Corneal Calcification in Hypercalcemia. Roentgenologic Findings... 609
- KING, NORMAN E. Suppurative Sialadenitis Produced by a Foreign Body in the Hypopharynx 609
- BREWER, DAVID W. Hypopharyngeal Polyp.... 609
- WALTNER, JULES G. Roentgen Diagnosis of Cholesteatoma of the Middle Ear..... 610

#### The Chest

- STEINMANN, ERIK P. On the Clinical Significance of Respiratory Motion of the Bifurcation in Lung Diseases..... 610
- CALDER, E. Fluoroscopic Preselection of the Tomographic Plane in Chest Lesions, with a Note on the Use of a Double Grid..... 610
- CASSELS, DONALD E., ET AL. Congenital Cystic Disease of the Lung..... 610
- VOLLMER, HERMANN. Chronic Emphysematous Cavity of the Lung..... 610
- DOONEIEF, ALFRED S., AND PICCAGLI, RUTH W. Lung Trauma at Pneumothorax Induction.. 611
- FRECKER, BRIAN E. Two Cases of Foreign Body in the Left Main Bronchus in Children..... 611
- GELFAND, MICHAEL. Paraffin Pneumonia..... 611
- BOUCOT, KATHARINE R., ET AL. Chest X-Ray Surveys in General Hospitals, a Critical Survey..... 611
- TURNER, H. MIDGLEY, AND MARTIN, W. J. Mortality and Survival Rates in Males with Silicosis or Silico-Tuberculosis..... 612
- PREUSS, FRED S. An Unusual Case of Anthracosilicosis..... 612
- HOGUE, WARREN L., JR., AND MALLETTE, FREDERICK S. A Study of Workers Exposed to Talc and Other Dusting Compounds in the Rubber Industry..... 613
- FURCOLOW, MICHAEL L. Development of Calcification in Pulmonary Lesions Associated with Sensitivity to Histoplasmin..... 613
- KNEIDEL, JOHN H., AND SEGALL, HAROLD. Acute Disseminated Histoplasmosis in Children... 613

- NORMAN, IRWIN L., AND LAWLER, ARTHUR L. Coccidioidomycosis..... 613
- McCORT, JAMES J. Infectious Mononucleosis, with Special Reference to Roentgenologic Manifestations..... 613
- NESTMANN, RALPH H. Sarcoidosis: Review of 11 Cases Including 2 Autopsies..... 614
- BRAWLEY, R. W., AND MODERN, F. W. S. Q Fever in a Veterans' Hospital..... 614
- SMITH, ROBERT R., ET AL. Terminal Bronchiolar or "Alveolar Cell" Cancer of the Lung..... 614
- VANÉK, JOSEF. Multinodular Carcinoma of the Lungs..... 614
- MAIER, HERBERT C. Intrathoracic Pheochromocytoma with Hypertension..... 615
- TOUROFF, ARTHUR S. W., AND SAPIN, SAMUEL O. Solitary Intrathoracic Neurofibroma..... 615
- PITTMAN, HELEN S., AND SCHATZKI, RICHARD. Pulmonary Effects of the Coconut Grove Fire. A Five-Year Follow-Up Study..... 615
- AISNER, MARK, AND FRANCO, JOHN E. Medical Progress. Mediastinal Emphysema..... 615
- MADER, VICTOR O., ET AL. Ciliated Columnar Epithelial Cyst of the Mediastinum..... 616
- HAUCH, EDWARD W., AND SITTLER, W. WALTER. Fibromyxoma of the Pleura..... 616
- JÖNSSON, GUNNAR, ET AL. Selective Angiocardiography..... 616
- BRODÉN, BROR, ET AL. Thoracic Aortography... 616
- STEINBERG, ISRAEL, ET AL. Angiocardiographic Diagnosis of Syphilitic Aortitis..... 617
- THORNER, M. C., ET AL. Calcification as a Diagnostic Sign of Syphilitic Aortitis..... 617
- MILLER, JOSEPH H., AND WEDUM, BERNICE G. Cardiac Enlargement in Uncomplicated Mitral Insufficiency in Children..... 617
- SWAN, HENRY, ET AL. Criteria of Operability in Tricuspid Stenosis..... 618
- ERF, L. A., ET AL. Pulmonary Hemangioma with Pulmonary Artery-Aortic Septal Defect. Attempted Roentgen Visualization by Catheterization of Brachial Artery and Basilic Veins..... 618

#### The Digestive System

- CLIFFTON, EUGENE E. Spontaneous Rupture of the Esophagus..... 618
- FRACASSO, E., AND GURIAN, G. Periesophageal Thickening Following Ingestion of Lye.... 618
- HEALY, MARTIN J., JR., AND SAUER, PAUL K. Some Limitations of Vagotomy in the Treatment of Peptic Ulcer..... 618
- SCHROEDER, C. MORRISON. Hourglass Stomach Caused by Annular Muscular Hypertrophy.. 619
- WALK, L. Phytobezoar in the Gastric Stump... 619
- CRENSHAW, JAMES F. Cholecystocolic Fistula... 619

- KLEITSCH, W. P., ET AL. Diaphragmatic Hernia with Complete Evisceration of the Liver.... 619

### The Musculoskeletal System

- SCATCHARD, G. NEWTON. Orthopedic X-Ray Problems in Children..... 620
- ENGEL, MILTON B., ET AL. Mandibular Growth Disturbance in Rheumatoid Arthritis of Childhood..... 620
- PROFFITT, JAMES N., ET AL. Fibrous Dysplasia of Bone..... 621
- PERRUELO, NICOLÁS N., AND ROSSI, PABLO. Fibrous Dysplasia of a Rib..... 621
- HACKETT, LOUIS J., JR., AND CHRISTOPHERSON, WILLIAM M. Polyostotic Fibrous Dysplasia..... 622
- FAIRBANK, H. A. THOMAS. Cranio-Cleido-Dysostosis..... 622
- FAIRBANK, H. A. THOMAS. Achondroplasia..... 622
- TURKISH, MARTIN, ET AL. Osteitis Tuberculosa Multiplex Cystica..... 623
- BEACH, EDWARD W. Osteitis Pubis: A Urologic and Roentgenographic Study..... 623
- KRAININ, PHILIP, ET AL. Multiple Myeloma with New Bone Formation..... 623
- POKORNÁ, LILLY. Roentgen Diagnosis of Osteoporosis, in the Concentration Camp at Theresienstadt..... 624
- FITTS, WILLIAM T., ET AL. Effect of Intramedullary Nailing on the Healing of Fractures. An Experimental Study..... 624
- DENSTAD, TORFINN. Resorption of Abrodil in Myelography..... 624
- JAMES, E. S., AND DECTER, P. H. The Cervical Disc Syndrome..... 624
- KNUTSSON, FOLKE. Fusion of Vertebrae Following Non-Infectious Disturbance in the Zone of Growth..... 624
- HARRIS, H., AND JOSEPH, J. Variation in Extension of the Metacarpo-Phalangeal and Interphalangeal Joints of the Thumb..... 625
- RUSHFORTH, A. F. A Congenital Abnormality of the Trapezium and First Metacarpal Bone..... 625
- LASSERRE, CH., ET AL. Osteoarthritis of the Trapezio-Metacarpal Joint..... 625
- SYLWAN, TORE. Impression Fractures in the Caput Humeri in Connection with Electroshock..... 625
- CURR, J. F. Synovial Osteochondromatosis..... 626

### Gynecology and Obstetrics

- BROWN, WILLIS E., ET AL. Absorption of Radiopaque Substances Used in Hysterosalpingography. A Comparative Study of Various Aqueous and Oily Media..... 626
- KÄSER, O., AND DEUEL, H. Experience with Hysterosalpingography (Exclusive of Tubal Patency in Sterility)..... 626
- BERGMAN, R. THEODORE. Diverticula of the Female Urethra..... 627
- MARCHETTI, ANDREW A. Female Bladder and

- Urethra Before and After Correction for Stress Incontinence..... 627
- MALPAS, P., ET AL. Displacement of the Bladder and Urethra During Labour..... 627
- CREWS, H. R., ET AL. Value of Upright Roentgenograms of the Maternal Pelvis at or Near Term with Particular Reference to Placenta Praevia..... 627

### The Genito-Urinary System

- ABESHOUSE, BENJAMIN S. Renal and Ureteral Fistula of the Visceral and Cutaneous Types..... 628
- ENGEL, WILLIAM J. Intravenous Urography in the Study of Vesical Neck Obstructions.... 629
- HEYMANN, WALTER, AND MARTIN, JAMES F. Bilateral Megalo-Ureter in a Child..... 629

### Technic; Contrast Media

- RESINK, J. E. J. Is a Roentgenogram of Fine Structures a Summation Image or a Real Picture?..... 629
- RADNER, STIG. Subclavian Angiography by Arterial Catheterization. Visualization of Metastatic Tumor in the Upper Thoracic Aperture..... 630
- HÖJENSGÅRD, I. C. Phlebography in Chronic Venous Insufficiency of the Lower Extremity..... 630
- MORGAN, RUSSELL H. Electrocardiography. Progress of Medical Science..... 630
- HELLSTRÖM, B., AND HOLMGREN, HJ. Reaction of the Lung on Bronchography with Viscous Umbradil (Umbradil-Viskös B) (Astra), Umbradil (Astra), and Carboxymethyl Cellulose. An Experimental Investigation on Animals..... 630
- HYDE, LEROY, AND HYDE, BERNARD. Effect of Retained Bronchial Lipiodol on Blood Iodine..... 630
- CREPEA, SEYMOUR B., ET AL. Failure of Antihistaminic Drugs to Inhibit Diodrast Reactions..... 631
- MOORE, SHERWOOD. Training of the Blind for Dark Room Technicians..... 631

### RADIOTHERAPY

- STETSON, CHARLES G., AND SCHULZ, MILFORD D. Carcinoma of the Eyelid. Analysis of 301 Cases and Review of the Literature..... 631
- FOWLER, ROBERT, AND MCCALL, CYNTHIA. Results of Surgical and Radiological Treatment in Primary Carcinoma of the Breast..... 631
- HENRIKSEN, ERLE. Lymphatic Spread of Carcinoma of the Cervix and of the Body of the Uterus..... 632
- McKELVEY, J. L., ET AL. Results of an Experimental Therapy of Carcinoma of the Cervix..... 632
- EVERETT, HOUSTON S., ET AL. Further Studies on the Effect of Irradiation Therapy for Carcinoma of the Cervix upon the Urinary Tract..... 632
- MUNNELL, EQUINN W., AND TAYLOR, HOWARD C., JR. Ovarian Carcinoma. Review of 200 Primary and 51 Secondary Cases..... 633

JACOBS, MELVILLE L. Testicular Tumor and the Status of Radiation Therapy.....	633
RONCHESI, F. Radium in Treatment of Hemangioma.....	633
ALDERS, NICHOLAS. Cavernous Haemangioma of the Perineum.....	634
KÖRBLER, JURAJ. Radioresistant Hemangiomas.....	634
OLIVER, EDWARD A., ET AL. Eosinophilic Granuloma of the Skin.....	634
ANDERSEN, POUL E. Extramedullary Plasmocytomas.....	634
SNEAD, CLAUDE R., ET AL. Roentgen Therapy of Thrombophlebitis.....	634
BRADLEY, J. EDMUND, AND DRAKE, MILES E. Effects of Preoperative Roentgen-Ray Therapy on Arterial Hypertension in Embryoma (Kidney).....	635
COURT BROWN, W. M. Wide Field Irradiation and the Platelet Count.....	635

#### RADIOISOTOPES

LOWREY, GEORGE H., ET AL. Radioiodine Uptake Curve in Humans. Studies in Children....	635
TRUNNELL, J. B., ET AL. Treatment of Metastatic Thyroid Cancer with Radioactive Iodine.....	636
FITZGERALD, PATRICK J., AND FOOTE, FRANK W., JR. The Function of Various Types of Thyroid Carcinoma as Revealed by the Radioautographic Demonstration of Radioactive Iodine ( $I^{131}$ ).....	636
DOBYNS, BROWN M., ET AL. Method for the Preoperative Estimation of Function in Thyroid Tumors: Its Significance in Diag-	
nosis and Treatment.....	637
SEIDLIN, S. M., ET AL. Radioiodine Therapy of Metastases from Carcinoma of the Thyroid: A Six-Year Progress Report.....	637
POTTS, ALBERT M., ET AL. Effect of Thyroid Secretory Activity on the Distribution of Radioiodine in Plasma.....	637
FINCH, C. A., ET AL. Iron Metabolism. Erythrocyte Iron Turnover.....	637

#### RADIATION EFFECTS

WILLIAMS, KATHERINE, AND MARLEY, W. G. Discussion on the Physical, Cytological, and Medical Aspects of Protection from Ionizing Radiations with Special Reference to the Use of High-Voltage X-Rays and Radioisotopes.....	638
ZUGERMAN, I. Early Reactions Following Roentgen Ray Epilations.....	638
LEUCUTIA, T., AND COOK, JAMES C. Malignant Degeneration of Benign Giant Cell Tumor..	638
CRONIN, THOMAS D., AND BRAUER, RAYMOND, O. Radiodermatitis and Necrosis.....	639
GILES, ALAN M. Pregnancy Following Pelvic Irradiation.....	639
JACOBSON, L. O., ET AL. Effect of Spleen Protection on Mortality Following X-Irradiation	639
PATT, H. M., ET AL. Influence of Estrogens on the Acute X-Irradiation Syndrome.....	639
FREEMAN, BROMLIV S. Fluorescein as an Adjunct in the Treatment of Radionecrotic Ulcers....	640
SNELL, FRED M., ET AL. Hematologic Studies in Hiroshima and a Control City Two Years After the Atomic Bombing.....	640

## ROENTGEN DIAGNOSIS

## THE HEAD AND NECK

**A Review of Cerebral Angiography.** James W. D. Bull. *Proc. Roy. Soc. Med.* 42: 880-890, November 1949.

Cerebral angiography was first introduced in 1927 by Moniz using 25 per cent sodium iodide as a contrast material. Subsequently thorotrast was employed and later diodone (diodrast), which is now the most commonly used contrast material. At the outset only the surgical exposure technic was employed to any extent, but a percutaneous technic was developed in Norway in 1944 which places the procedure on an equal footing with pneumography, with which it competed for a number of years as a means of diagnosis of intracranial lesions.

As for safety, the author has had experience with some 500 odd cases with only 3 deaths within two days, but arteriography was not proved to be responsible in any of these. Occasionally there is a slight pyrexia for several days after the procedure, and a sore neck which is attributed to contrast material entering the carotid sheath and small hematomata. As one becomes more skilled with carotid arterial puncture, these complications are less likely to occur.

In considering drug (diodone) sensitivity the author likens the procedure to intravenous pyelography, which is done in many thousands of patients annually, nearly always without sensitivity tests. Since testing is not foolproof, one is probably justified in proceeding without any elaborate tests. Very rarely a large dose will cause a severe reaction or even death.

The only time anesthesia is employed is in uncooperative patients and in children. It is very desirable to have the patient conscious.

Lindgren (*Brit. J. Radiol.* 20: 326, 1947. *Abst. in Radiology* 51: 123, 1948) described the technic comprehensively. Following puncture of the common carotid, saline is injected slowly while preparations are made for the x-ray exposure. Ten cubic centimeters of contrast medium are then injected and three exposures are made at two-second intervals. The lateral films are usually taken first and the procedure is repeated for the anteroposterior views. The author emphasizes that no number of stereoscopic views will take the place of views in the right-angled planes.

Some of the indications for carotid angiography are clear-cut, while the value of the procedure in other instances depends upon judgment and experience. Vascular lesions of the brain must obviously be investigated primarily by angiography. The investigation of traumatic conditions is still in its infancy. Many tumors can be diagnosed by angiography, but pneumoencephalography is frequently a better method. As things stand at present, pneumoencephalography is the method of choice in investigating mid-brain and posterior fossa lesions. The indications for angiography are presented in five groups.

**Group A. Subarachnoid Hemorrhage:** This is now a clear-cut indication for angiography. Aneurysms are the commonest cause of subarachnoid hemorrhage but sometimes the aneurysm itself cannot be visualized. Sometimes a bleeding angioma may be encountered, and a case in which this occurred is presented. Bleeding tumors may be the cause.

**Group B. Arterial Occlusion:** Carotid thrombosis is

not so rare as is generally supposed. The two sites of election for the obstruction are about 2.5 cm. distal to the bifurcation of the common carotid and adjacent to the anterior clinoid process. An important point in angiography of such lesions is the visualization of the bifurcation of the common carotid. Emboli may be the cause of the obstruction.

**Group C. Craniocerebral Injury:** Angiography has been little used in cases of acute head injury but it has been reported useful. Lesions considered are: (1) extradural hematoma, (2) acute subdural hematoma, (3) intracerebral hematoma, and (4) cerebral edema.

**Group D. Sequela of Trauma:** Chronic subdural hematoma gives a pathognomonic appearance in a frontal arteriogram. The cerebral vessels are seen to be pressed inwards from the inner table. Arteriovenous fistula at the cavernous sinus is a rare sequel to trauma.

**Group E. Intracranial Expanding Lesions (Non-Traumatic):** Certain large aneurysms and angiomas are included in this group. Meningiomas frequently will fill with contrast material and there is a lag before the tumor empties, so that a so-called "blush" is seen on phlebograms. Normally all the medium has left the brain in five seconds. Unfortunately all meningiomas do not show this "blush" and some malignant gliomas do.

In malignant gliomas classically one sees many small abnormal vessels having the appearance of minute arteriovenous aneurysms which are sometimes best shown on phlebograms. This is not a reliable sign. It was seen in only 23 out of 36 cases, but when it is seen, it can be very important.

In metastases one may see small arteriovenous aneurysms similar to those seen in malignant gliomas. Usually the periphery of a metastatic lesion is better outlined than that of a glioma, and if there are multiple lesions the diagnosis is virtually certain.

Avascular expanding lesions such as benign glioma, abscess, and granuloma manifest themselves by vessel displacement. However, since there is such a wide variation of normal in cerebral vessels, detection of displacement may be very difficult.

The article is accompanied by a diagram of the normal carotid tree, 7 excellent reproductions of angiograms, and a photograph of a brain specimen.

J. D. CALHOUN, M.D.  
University of Arkansas

**Intracranial Tumours in the Aged.** Joe Pennybacker *Edinburgh M. J.* 56: 590-600, December 1949.

A review of cases of intracranial tumor seen at the Radcliffe Infirmary, Oxford, disclosed 86 in patients over the age of sixty. Of the tumors, 45 per cent were of the glioma series, and more than half of this group were spongioblastoma multiforme, which is one of the most malignant types. Metastatic cancer accounted for 15 per cent of the cases, the lung coming first as the primary site. The remaining cases comprised a miscellaneous group of acoustic neurinomas, pituitary tumors, and meningiomas, adding up to a significant total of 40 per cent, significant because these tumors are essentially benign and remediable.

It is of interest that in 83 per cent of the entire series the lesion was above the tentorium.

Intracranial tumors in the aged do not conform to the more familiar clinical picture seen in children and young adults, notably in that pressure signs and symptoms may occur late or not at all. The difficulties of diagnosis are enhanced by the fact that other diseases, especially cardiovascular disease, may produce signs and symptoms very much like those of brain tumors, and the differential diagnosis may demand all the refinements of modern medicine.

Roentgenograms of the skull are generally of little help unless they show displacement of the calcified pineal gland, which indicates an expanding lesion in one or other cerebral hemisphere. In most cases ventriculography will give the answer. The introduction of arteriography has been another step forward. With this procedure, the presence and location of a tumor, as well as its nature, can be determined, since different types of tumor have different vascular patterns. In some situations arteriography may not give as much or any more information than ventriculography, and commonly both procedures have to be employed.

About 60 per cent of the author's series were malignant in the sense that they could not be completely removed, and surgery had little to offer except palliation. In the remaining 40 per cent the results of operation were as good as in the younger age groups, and they justify the slightly greater risk of any major procedure in old age.

Four roentgenograms; 1 photograph; 2 tables.

**Brain Tumors in Children. I. General Considerations.** A. Earl Walker and Theron L. Hopple. *J. Pediat.* 35: 671-687, December 1949.

Intracranial tumors in children are located predominantly beneath the tentorium. Tumors of the medulla, pons, and third ventricle are much more common in childhood than in adult life. Because the majority of neoplasms in childhood are located along the neural axis and thus produce an internal hydrocephalus, the symptoms of increased intracranial pressure, vomiting, and headache are the most common early manifestations.

Roentgenograms of the skull may reveal diastasis of the sutures, intracranial calcification, calvarial distortion or erosion. The authors believe that special views of the optic foramen should be taken routinely. Angiography is of great help, when possible, in determining the location and type of tumor. Pneumoencephalography is a safe and valuable procedure in the absence of intracranial hypertension. With increased intracranial pressure, ventriculography is preferable to encephalography but carries a very definite risk in children. The authors discuss briefly the use of radioactive diiodofluorescein and phosphorus in the localization of tumors.

The mass of the tumor within the intracranial cavity is compensated for by (1) a decrease in the cerebrospinal and ventricular fluid, (2) a decrease in the amount of interstitial fluid within the brain, and (3) a decrease in the amount of intracranial blood.

Brain tumors must be differentiated from congenital abnormalities, inflammatory and toxic conditions, vascular disturbances, and traumatic lesions.

The paper is based on a series of 100 brain tumors in children.

Eight roentgenograms; 1 chart; 1 drawing.

HOWARD L. STEINBACH, M.D.  
University of California

**Pressure Changes in the Sella Turcica in the Presence of Glioma in the Cerebral Hemispheres.** Bengt Nordmark. *Acta radiol.* 32: 461-467, Dec. 31, 1949.

If and to what extent pressure changes in the sella turcica occur in the case of different gliomas is disputed. In order to throw some light upon this question, the author studied a series of 199 cases of glioma, including only those in the cerebral hemispheres, in order to preclude the possibility of pressure changes as the result of a dilated third ventricle.

The 199 cases were made up of 119 malignant gliomas, constituting almost two-thirds of the material, 64 astrocytomas, and 16 oligodendrogliomas. The most common site was in the frontal and temporal lobes. A smaller number of tumors were located in the parietal lobes and a few in the occipital lobe.

Pressure changes in the sella occurred in 100 per cent of the cases in which the tumor was in the occipital lobe, though in view of the small number of cases—only 7—this may be a coincidence. Glioma in the other lobes was accompanied by pressure changes in the sella turcica in approximately 50 per cent of the cases. With malignant glioma in the parietal lobe, changes occurred in 70 per cent. From these observations, the author concludes that no obvious differences, as to the incidence of pressure changes with varying tumor localization were present in this material.

With malignant glioma, there were pressure changes in the sella turcica in 58.8 per cent of the cases and with benign gliomas in 56.2 per cent. Thus the occurrence of pressure changes in the sella does not justify any conclusions regarding the malignancy of an established tumor.

The various changes which occur within the sella are described.

Six roentgenograms; 1 table.

F. R. McCREA, M.D.  
Indiana University

**Subdural Hematoma and Effusion in Infants. Review of Fifty-Five Cases.** Arthur R. Elvidge and Ira J. Jackson. *Am. J. Dis. Child.* 78: 635-658, November 1949.

The authors have analyzed 55 consecutive cases of subdural effusion and hematoma in infants. These they have divided into four groups, namely definite birth injuries, probable birth injuries, post-natal head injuries, and an unclassified group. The stress and strain on the fetal head during molding are the greatest factor in the production of trauma. Thus, what appears to be a normal labor and delivery may be sufficient to cause intracranial damage.

Any infant with hydrocephalus or seizures should be suspected of having a subdural effusion. When the state of consciousness is disturbed and there are abnormal neurologic findings following a recent head injury, whether it is natal or post-natal, the diagnosis of subdural effusion becomes more obvious. Some of the patients also exhibit vomiting, malaise, hyperthermia, and drowsiness.

Subdural puncture is the only method of making an accurate diagnosis. The anterior fontanelle appears to be the most practical site for puncture in the average child. The presence of bloody fluid is evidence of recent hemorrhage, while xanthochromic fluid indicates old hemorrhage.

Roentgenograms of the skull may reveal a fracture or separation of the suture lines.

the Pres-  
es. Bengt  
11, 1949.

in the sella  
mas is dis-  
is question,  
glioma, in-  
spheres, in  
changes as

nt gliomas,  
al, 64 astro-  
most com-  
lobes. A  
the parietal

00 per cent  
the occipital  
of cases—  
in the other  
in the sella  
the cases.  
ne, changes  
ations, the  
ferences, as  
ying tumor

ure changes  
es and with  
occurrence  
justify any  
established

the sella are

EA, M.D.  
university

ants. Re-  
ge and Ira  
November

ve cases of  
ts. These  
ly definite  
natal head  
stress and  
the greatest  
y, what ap-  
e sufficient

s should be  
When the  
ere are ab-  
t head in-  
agnosis of  
ome of the  
berthermia,

making an  
appears to  
the average  
ence of re-  
l indicates

fracture or

In the hydrocephalic infant, pneumography is of special value in the diagnosis of the degree and type of hydrocephalus and of the existence of subdural effusion. It is useful after an operative procedure in order to estimate the amount, if any, of residue in the subdural space, to determine a shift of mid-line structures, or to follow the degree of ventricular dilatation or cerebral atrophy. If ventricular dilatation and increased pressure exist, ventriculography by way of the anterior fontanelle is the method of choice. If the infant is small, it is inadvisable to do a ventricular puncture because of the possibility of producing unnecessary damage to the brain.

The surgical treatment consists of emptying the subdural space and completely removing the membranes when they are present. The acute subdural hematoma, as in the group with definite birth injuries, is best treated by aspiration, for no membrane is usually present at this early stage. The chronic subdural effusion is most satisfactorily treated by trepanation for identification of membranes and, if their presence is confirmed, by early complete removal of the inner membrane.

Careful attention to the fluid and protein balance in the management of these infants will aid greatly in reducing the operative mortality.

Thirteen roentgenograms; 2 photographs; 2 tables; 4 charts.

DANIEL WILNER, M.D.  
Atlantic City, N. J.

**Conjunctival and Corneal Calcification in Hypercalcemia. Roentgenologic Findings.** Felix G. Fleischer and Seymour R. Shalek. *New England J. Med.* 241:863-865, Dec. 1, 1949.

This paper reviews the literature on ocular calcification and reports the case of a 42-year-old male with crippling polyarthritis for twenty years, who had received vitamin D medication since 1942. Blood and gravel were passed in the urine on several occasions beginning in 1943. In 1949, x-ray examination of the abdomen showed bilateral calcification of the kidneys. At that time, the thyroid gland was found to be about three times normal size; the chest showed bilateral calcified tuberculosis and emphysema; and there was advanced rheumatoid arthritis in the joints of the extremities. No soft-tissue calcification was found in the extremities or in the walls of the chest or abdomen.

Ophthalmologic examination revealed calcification in the cornea and conjunctiva extending toward the limbus of the cornea on both the temporal and nasal sides of both eyes. Roentgenographic examination of the skull showed faint calcifications in annular arrangement in the orbit. With bone-free technic these were shown in better detail. The technical factors used for the latter procedure are about the same as for radiography of the front teeth: 15 ma., 55 kv., 1 second. Dental films are used, the film being inserted along the nasal side of the eye, and the tube centered toward the outer canthus from behind.

Three possible etiologic factors were considered in this case: hyperparathyroidism, overdosage of vitamin D, and immobilization due to rheumatoid arthritis. In these conditions, soft-tissue calcifications are known to be quite common. The parathyroid region was explored, but no tumor was found.

Three roentgenograms; 1 drawing.

JOHN B. MCANENY, M.D.  
Johnstown, Penna.

**Suppurative Sialadenitis Produced by a Foreign Body in the Hypopharynx. Report of an Unusual Case.** Norman E. King. *Arch. Otolaryng.* 50: 827-830, December 1949.

A case is presented in which a foreign body, a toothbrush bristle, had apparently entered the left peritonsillar fossa and dissected laterally into the neck, setting up an inflammatory process which extended anteriorly to the submaxillary gland and duct and produced sialadenitis and a through-and-through sinus tract extending from the tonsillar fossa to the frenulum of the tongue.

The patient, a 26-year-old army lieutenant, was seen numerous times over an eighteen-month period. At first he complained of a pricking sensation in the left tonsillar area and a "hard lump" under the left side of the mandible in the region of the submaxillary gland. No calculi or opaque foreign body could be demonstrated roentgenologically. A peritonsillar abscess was incised and a moderate amount of pus liberated. Shortly thereafter an injection of lipiodol into Wharton's duct revealed a small amount of oil extending along a narrow tract posterior to the gland and pocketing into the soft tissues at the angle of the jaw. The gland itself was not outlined by the medium. Tonsillectomy was performed.

During the postoperative course, pressure on the submaxillary gland produced drainage of creamy yellow pus from the middle of the left tonsillar fossa and from Wharton's duct. About six months postoperatively injection of lipiodol through the sinus opening in the left tonsillar fossa disclosed a sinus tract contiguous with the left submaxillary gland and Wharton's duct. Injection of methylene blue through the same opening revealed that the dye was expelled freely at the frenulum of the tongue, thus demonstrating a free and continuous communication.

The posterior sinus tract was excised, and an ordinary toothbrush bristle was removed. The patient made an uneventful recovery.

**Hypopharyngeal Polyp.** David W. Brewer. *Arch. Otolaryng.* 50: 831-832, December 1949.

A case of hypopharyngeal polyp in a 55-year-old woman is reported. The patient complained of nausea, associated with the feeling of a moving lump in the throat, and stated that on two occasions a long, thick, red object was regurgitated and hung out of the mouth to the chin. Initial examination showed nothing abnormal. Five minutes later, a second indirect laryngoscopy revealed a small rounded polypoid mass lying in the left piriform sinus. Roentgen examination with a barium swallow disclosed a smooth, elongated, sausage-like filling defect in the upper half of the esophagus. This soft-tissue mass apparently arose near the region of the cricopharyngeal muscle and extended down the esophagus for a distance of approximately 18 cm., or just below the arch of the aorta. There was no evidence of ulceration of any portion of the esophagus, and the mass was therefore considered to be benign. The hypopharynx and esophagus were otherwise not remarkable.

A polyp measuring 13.5 cm. in length, 3 cm. in diameter in its midportion, and 2 cm. in diameter at the pedicle was removed. The microscopic diagnosis was benign fibromatous polyp.

One roentgenogram; 1 photograph of specimen.

**Roentgen Diagnosis of Cholesteatoma of the Middle Ear.** Jules G. Waltner. *Am. J. Roentgenol.* 62: 674-684, November 1949.

As defined by the author, a "cholesteatoma is an epidermoid inclusion cyst which develops in the mastoid as a result of the extension of squamous epithelium into the middle ear through a perforation in the drum." Accurate roentgen diagnosis should be attempted in every case to (1) confirm the clinical diagnosis, (2) detect early cases still lacking clinical symptoms, and (3) determine the extent of the cyst. Because of the difficulties encountered in making the correct roentgen diagnosis the author made the study reported herein.

A study of 16 non-pneumatized mastoid specimens in serial sections showed the normal antrum to be wider than 6 mm. in its upper two-thirds, but never wider than this in its lower one-third. The upper limit of normal height was found to be 11 to 12 mm.

Roentgen studies of cholesteatoma of the middle ear lead to erroneous conclusions in about one-third of all operated cases. The majority of errors consist in failure to recognize roentgenologically a cholesteatoma subsequently found at operation.

Fifteen roentgenograms; 1 table.

J. B. SCRUGGS, M.D.  
University of Arkansas

## THE CHEST

**On the Clinical Significance of Respiratory Motion of the Bifurcation in Lung Diseases.** Erik P. Steinmann. *Schweiz. med. Wchnschr.* 79: 1126-1130 Nov. 26, 1949. (In German)

The author states that respiratory motion of the carina, pendulum fashion, is a valuable diagnostic sign, readily observed at bronchoscopy. The normal respiratory motion is vertical, and about 8 to 10 mm. in range; there is no appreciable lateral shift. Acceleration of the respiratory stream in either lung as a result of disease, bronchostenosis, etc., and the existence of an intact pleural space leads to an inspiratory shift to the homolateral side. A similar shift occurs in pneumothorax. With obliteration of the pleural space, the shift is to the contralateral side, in the absence of pulmonary disease; the pleural shift tends to mask the effects of a concomitant pulmonary or bronchial affection. Twelve drawings show the roentgen findings.

LEWIS G. JACOBS, M.D.  
Oakland, Calif.

**Fluoroscopic Preselection of the Tomographic Plane in Chest Lesions, with a Note on the Use of a Double Grid.** E. Calder. *Brit. J. Radiol.* 22: 627-633, November 1949.

An ingenious method of locating chest lesions for the selection of the best tomographic plane is presented. At the fluorescent screen the patient is rotated until the lesion is most clearly visualized. He is then rotated 90 degrees and a lead strip is affixed to the skin coinciding with the middle of the shadow of the lesion. After further rotation of 180 degrees, another centrally located lead strip is affixed to the skin. The plane of the central ray when these are superimposed corresponds with the plane which will be horizontal and will cut the lesion when the patient is positioned on the tomographic table.

A double grid method is also advocated. A stationary grid is placed upon the table top with the strips

perpendicular to the strips of a movable grid. This requires the addition of about 8 more kilovolts than would normally be used. It increases the contrast in the center of the film and obliterates many of the distorted shadows at the periphery.

Fourteen roentgenograms; 3 diagrammatic drawings.  
SYDNEY J. HAWLEY, M.D.  
Seattle, Wash.

**Congenital Cystic Disease of the Lung.** Donald E. Cassels, James M. Fritz, and W. E. Adams. *J. Pediat.* 35: 585-600, November 1949.

Congenital cystic disease of the lung is attributable to a failure of the terminal respiratory passages to reach proper maturity and the formation, instead, of blind, non-rigid, tube-like rests. Depending upon the number of bronchi involved, there may be a solitary cyst or multiple cysts. These cystic spaces usually communicate with the bronchial tree through small bronchi which may be difficult or impossible to demonstrate grossly or histologically.

Clinical manifestations arise occasionally from distention of the cyst or cysts, with compression of adjacent pulmonary structures, but usually are the result of superimposed infection.

The authors present 6 cases of congenital cystic disease of the lung. Five of these were confused with empyema, lung abscess, bronchiectasis, chronic non-specific pneumonitis, and pulmonary tuberculosis, respectively. In the sixth case, the correct diagnosis was made on the basis of the roentgen examination.

Suspicion of the presence of cystic disease should be aroused by (1) chronic pulmonary suppurative disease which does not respond to treatment, (2) areas of pneumonitis and infiltration which are not tuberculous and do not respond to treatment, and (3), in occasional instances, by suggestive roentgen findings.

Sixteen illustrations, including 10 roentgenograms.

HOWARD L. STEINBACH, M.D.  
University of California

**Chronic Emphysematous Cavity of the Lung.** Hermann Vollmer. *Am. J. Dis. Child.* 78: 755-758, November 1949.

The author presents a twenty-one-year follow-up report on what appears to be an emphysematous cavity in the right lung. In November 1926, at the age of five and a half years, the patient had a fever for twelve days and a non-productive cough. Thereafter her temperature remained normal. However, she made a slow recovery, continued to cough, and appeared chronically ill. A roentgenogram of the chest in March 1927 showed a dense, round infiltration in the right hilar region. In June 1927, a large cavity with an air-fluid level was apparent. Roentgenograms of the chest in January and March 1928 showed no essential change. In view of negative cutaneous and intracutaneous tuberculin tests, a diagnosis of unspecific cavity following a chronic pulmonary infection was made. During the following ten years, the girl was in good health. A routine roentgenogram of her chest in 1948 revealed a cavity in the right lung with an air-fluid level. Fluoroscopically, a sharply circumscribed cyst, 33 to 39 mm. in diameter, was visible at the base of the upper lobe of the lung, surrounded by normal pulmonary tissue. Fluid filled about half of the cavity and the level shifted with change in position.

On the basis of the available data, the nature of this cavity cannot be determined with certainty. Differential diagnostic considerations included congenital cyst, tuberculous cavity, pulmonary abscess, loculated pneumothorax, and echinococcus cyst. The clinical data, laboratory tests, and roentgen criteria tended to rule out these diagnoses, however, leaving as the most acceptable interpretation of this case, an emphysematous cavity distal to a bronchial obstruction of the check-valve type, due to a pulmonary infection.

Benjamin and Childe, as well as Caffey, encountered 39 emphysematous cysts. All these cases were associated with or followed a respiratory infection, were asymptomatic, and cleared up spontaneously.

The author's case, originally reported in 1928 (*Ztschr. f. Kinderh.* 46: 810, 1928), is one of the first in the literature and has the longest follow-up period. It teaches that not all emphysematous cavities disappear spontaneously but that, nevertheless, a conservative attitude is to be recommended.

Two roentgenograms.

DANIEL WILNER, M.D.  
Atlantic City, N. J.

**Lung Trauma at Pneumothorax Induction.** Alfred S. Dooneief and Ruth W. Piccagli. *Am. Review Tuberc.* 60: 557-563, November 1949.

The study reported was undertaken because of a severe tension pneumothorax which developed in a case of pulmonary tuberculosis following induction of therapeutic pneumothorax. It was felt that lung trauma was the important factor in this case.

In an attempt to determine the incidence of trauma to the lung during induction of therapeutic pneumothorax in tuberculosis, a series of 23 consecutive patients was studied. The patients were prepared for induction of pneumothorax and, following intrapleural readings which indicated that the needle was in the pleural space, it was withdrawn without introducing any air. Chest roentgenograms were taken in expiration at intervals of three, six, and twenty-four hours after the procedure. After the last film had been taken, the procedure was repeated and pneumothorax was induced; all pleural spaces were shown, by the pressure readings and by successful induction of pneumothorax following the study, to be unobliterated.

Two of the 23 patients showed evidence of pneumothorax after the needling alone; it amounted to about 10 per cent collapse of the right upper lobe in one case and 20 per cent collapse of the right upper lobe in the other. No symptoms were noted in either case. It is possible that there was enough lung injury in some of the other cases to produce a pneumothorax so small that visualization was not possible; if so, it was probably of no clinical significance.

Despite reports to the contrary, it is evident that pneumothorax can be induced in the majority of patients with pulmonary tuberculosis without significant lung trauma.

Two tables.

JOHN H. JUHL, M.D.  
University of Wisconsin

**Two Cases of Foreign Body in the Left Main Bronchus in Children.** Brian E. Frecker. *M. J. Australia* 2: 713-714, Nov. 12, 1949.

The author presents two similar cases of foreign body in the left main bronchus, which might easily have been

overlooked on the evidence of a single film taken at full inspiration. Valvular block leading to hyperinflation is the commonest early finding in cases of bronchial obstruction in children, and the single film at full inspiration may appear quite normal or show only slight over-inflation of the affected lung or lobe. Fluoroscopy overcomes this difficulty and should not be omitted in the examination of young children. An additional film on expiration would give most of the information obtained by fluoroscopy, but in very young children it may be difficult to obtain films at a chosen stage of respiration.

X-ray examination of the chest in each case showed practically identical findings. There appeared to be a patchy atelectasis of the right lung which was thought to be due either to widespread bronchopneumonia or to a foreign body impeding air entry in the right main bronchus. Fluoroscopy, however, revealed a valvular block of the left main bronchus. A to-and-fro movement of the lower part of the mediastinum was evident under the screen, movement being toward the right on expiration and back to the normal mid-line position on full inspiration. That is to say, the left lung was in a condition of fixed inflation. The left dome of the diaphragm had a greatly diminished range of movement, being practically fixed at its inspiratory limit. In each case, bronchoscopy revealed half a peanut, surrounded by mucosal swelling, in the left main bronchus.

Four roentgenograms.

DANIEL WILNER, M.D.  
Atlantic City, N. J.

**Paraffin Pneumonia.** Michael Gelfand. *Brit. M. J.* 2: 1151-1152, Nov. 19, 1949.

The author presents 5 cases of paraffin (kerosene) pneumonia and reviews the literature on the subject. Some experimental studies point to kerosene aspiration as the cause of the pulmonary findings both clinically and radiographically, while other work supports the theory of a primary vascular damage through absorption in the blood stream to account for the changes in the bronchi.

Much of the paper is devoted to a summary of Steiner's work (*Am. J. Dis. Child.* 74: 32, 1947). Steiner classified his cases into three groups on the basis of severity and complications: (1) acute toxicity and depression of the central nervous system, with minimal pulmonary changes, followed by rapid recovery; (2) severe pneumonia and hyperpyrexia, with prolonged recovery; (3) severe pneumonia, with evidence of degenerative changes of the myocardium, liver, kidneys, and gastro-intestinal tract. The prognosis in an individual is held by Steiner to depend upon the following factors: (1) age, infants being more susceptible than adults; (2) amount of oil ingested; (3) extent of vomiting and aspiration; (4) nature and rapidity of the emergency treatment.

E. S. KEREKES, M.D.  
University of Arkansas

**Chest X-Ray Surveys in General Hospitals, a Critical Review.** Katharine R. Boucot, David A. Cooper, E. Wayne Marshall, and Fred MacD. Richardson. *Ann. Int. Med.* 31: 889-898, November 1949.

In December 1947, a study was made of the current effectiveness of hospital chest surveys in the Philadelphia area. An analysis was undertaken of the four 70 mm. photofluorographic units operating at Philadelphia General Hospital and at three teaching hos-

pitals. The following points were considered: (1) location of the unit, (2) its layout, (3) procedure, (4) staff, (5) record-keeping, and (6) follow-up.

The primary purpose of hospital chest surveys is the detection of infectious tuberculosis in order to protect hospital personnel and other patients. This achievement is accomplished only by prompt diagnosis, with isolation and appropriate treatment of cases uncovered by survey. If hospital surveys are to be effective, a high percentage of patients must report for photofluorography at admission. It is obvious that examination on discharge cannot protect contacts.

An analysis of admissions at the largest of the four hospitals revealed that 50 per cent were made during hours when the unit was not in operation. At this hospital, during October 1947, 1,011 individuals were admitted during hours when the unit was closed, and of these, 495 were too ill to report to the unit when subsequently sent for. This suggests that an important reason for failure to obtain roentgenograms of all admissions lies in the fact that the unit was not open around the clock.

One of the four units had a satisfactory follow-up program, but even this was not fully effective in actual practice. Record-keeping was seriously inadequate at all four units. Consequently it was not possible to evaluate the real service rendered by these units to their respective hospitals.

In their recommendations, the authors state that while the taking and reading of photofluorograms quite rightly belongs under the jurisdiction of the X-ray Department, the follow-up belongs under the Department of Chest Diseases. They recommend further that the taking, processing, reading, and reporting of photofluorograms be carried out within twenty-four hours; that a periodic check be made to insure that all patients are being referred for photofluorograms; that provision be made for the taking of photofluorograms around the clock, seven days a week; that prenatal cases and individuals scheduled for operations of election be referred to the unit before admission, and that accident cases, patients having emergency operations, and children too young to co-operate be sent *via* stretcher to the regular X-ray Department; that patients too ill to be examined by x-ray have special studies for tubercle bacilli if sputum be available; that the hospital office be instructed not to discharge any patient who has not had a photofluorogram; that correlation of subsequent clinical reports be prompt and routine, providing a valuable source of teaching material.

Four roentgenograms.

STEPHEN N. TAGER, M.D.  
Urbana, Ill.

**Mortality and Survival Rates in Males with Silicosis or Silico-Tuberculosis.** H. Midgley Turner and W. J. Martin. *Brit. M. J.* 2: 1148-1150, Nov. 19, 1949.

There are few published data on the expectation of life in silicosis and silico-tuberculosis. In silico-tuberculosis the prognosis is obviously dominated by the tuberculous element. In silicosis alone life expectation is important in connection with either life insurance or compensation, but few physicians see sufficient cases to establish criteria.

The data upon which the paper is based have been accumulated during a period of nineteen years. The series consists of 814 men with silicosis or silico-tubercu-

losis, each of whom reached the age of forty and had the opportunity of reaching the age of forty-one or more. The age of forty was used as the commencing age in the series because silicosis is a condition which develops gradually as a result of an occupational hazard over a period of years. The proportion of cases in which it is possible to diagnose silicosis with certainty below the age of forty varies with different processes but is comparatively small. After the age of forty this proportion increases fairly rapidly.

In the series reported, the chances of a case originally diagnosed as pure silicosis later developing tuberculosis proved to be only 6 per cent. However, the original separation of cases was in the following ratio: silicosis to silico-tuberculosis 348 to 466. A further breakdown of the ratio of so-called pure silicosis to infected silicosis apparently differs with the various trades or occupations of the individuals.

In their discussion, the authors point out that tuberculosis, with or without the mention of silicosis, is given as the cause of death in a majority of the members of the series with silico-tuberculosis. The prognosis of a case of silicosis with tuberculosis is always serious. It is worse when the tuberculous infection occurs at the outset of the silicosis, it is worse in younger than in older subjects, and it is worse than in cases of tuberculosis alone.

A handicap in the treatment of silico-tuberculosis is that collapse therapy is rarely indicated or helpful. The majority of the patients are in their fifth or sixth decades, and there is often difficulty in judging the contralateral lung both with regard to its functional capacity and also the presence of active tuberculous lesions.

The survival rates for males with silico-tuberculosis compare unfavorably at all ages over forty with the rates for males with pure silicosis or with the control rates for males in the general population. There is a reduction of thirteen years in life expectation at the age of forty for the group with silico-tuberculosis. Up to the age of fifty-one the survival rates for males with pure silicosis are similar to those of males in the general population. After the age of fifty-one there is an adverse deviation in survival rates for the group with pure silicosis. This results in a decrease in expectation of life of eight years from the age of forty as compared with the expectation of life for males in the general community.

Three tables; 1 graph. E. S. KEREKES, M.D.  
University of Arkansas

**An Unusual Case of Anthracosilicosis.** Fred S. Preuss. *New York State J. Med.* 49: 2667-2672, Nov. 15, 1949.

A case, unusual by virtue of the unorthodox histologic picture, is reported. Instead of the usual classically nodular or diffuse fibrosis of the lung parenchyma found in most cases of silicosis, these lungs revealed an extensive patchy organizing pneumonia and interstitial changes which, in spite of prolonged exposure to dust, resembled those found in the early stages of the disease. The chemical analysis showed 6.14 per cent silicon dioxide in dried lung tissue.

The importance of chemical analysis of lung tissue in definite and doubtful cases of silicosis is stressed.

Seven photomicrographs.

EDWARD E. LEVINE, M.D.  
Dearborn, Mich.

**A Study of Workers Exposed to Talc and Other Dusting Compounds in the Rubber Industry.** Warren L. Hogue, Jr., and Frederick S. Mallette. *J. Indust. Hyg. & Toxicol.* 31:359-364, November 1949.

A study was made in two rubber plants of workers exposed to talc and other dusting compounds for periods as long as thirty-six years. Complete physical examinations, including blood counts, urinalysis, blood pressure readings, and vital capacity determinations, were made. Chest roentgenograms on 14 × 17-inch films were interpreted by a qualified radiologist with considerable experience in the diagnosis of pneumoconiosis.

The two groups of workers included in the study were specially selected for type and length of exposure. The first group was composed of 20 men who had been exposed to talc alone for periods ranging from ten to thirty-six years. All of the men were working at the time of the study and were apparently in good health, and none presented any symptoms referable to the lungs. In this group the roentgen findings were either completely normal or showed only the chronic changes found in industrial urban dwellers. The second group was composed of 20 men with a major exposure to whiting and minor exposures to pyrophyllite and talc. The exposure periods of this group ranged from ten to twenty-five years. All of these men were also working at the time of the study and none had symptoms referable to the lungs. In this group only one chest roentgenogram showed abnormality, which was considered third-stage pneumoconiosis. This man had worked in the rubber industry for twenty-four years and had lost only three weeks from illness during that time. He had previously worked in coal mines for a period of five years.

The findings of the present study indicate that long exposure to talc does not appear to produce pathologic changes in the lungs.

Proposals that limits for silicate minerals be added to lists of maximum allowable concentrations should include careful definition of chemical and mineralogical composition.

Two roentgenograms; 4 tables.

**Development of Calcification in Pulmonary Lesions Associated with Sensitivity to Histoplasmin.** Michael L. Furcolow. *Pub. Health Rep.* 64: 1363-1393, Nov. 4, 1949.

In an earlier paper, Furcolow, Mantz, and Lewis (*Pub. Health Rep.* 62: 1711, 1947. *Abst. in Radiology* 51: 747, 1948) reported the demonstration of pulmonary infiltrates in a considerable number of histoplasmin-positive, tuberculin-negative children. These children have now been followed for varying periods up to four years, during which time some of the infiltrates have disappeared, some have apparently become fibrotic, and some—the majority—have gradually shown calcification. Seventeen cases of the last group form the basis of this paper.

The pre-calcific pulmonary infiltrates are classified as disseminated infiltrates, pneumonic infiltrates, and nodular foci. Disseminated infiltrates may be millet seed in size or may range from lesions a few millimeters in diameter to large conglomerate patchy areas. In some a central core of calcification may be seen. The calcifications, like the original lesions, are widely distributed throughout the pulmonary parenchyma and are of varying size and shape.

Pneumonic infiltration usually involves a small area,

poorly circumscribed and irregular in shape. The calcification appears as small scattered foci or as a single lesion in a clearing area.

Nodular lesions are demonstrable as well defined shadows from 1 to 4 cm. in diameter. A calcified central core is characteristic, though in some instances the calcium replaces the whole nodule or occurs in multiple small areas within the infiltrate.

Hilar adenopathy was seen in more than half the cases, with raspberry-like calcifications in some nodes and a fairly homogeneous deposit of calcium salts in others.

Fifty-six roentgenograms.

BERNARD S. KALAYJIAN, M.D.  
Detroit, Mich.

**Acute Disseminated Histoplasmosis in Children. Report of Three Cases.** John H. Kneidel and Harold Segall. *Pediatrics* 4: 596-603, November 1949.

The authors review the clinical and pathological aspects of histoplasmosis and report 3 cases. The roentgen findings are not diagnostic. Diffuse nodularity of the lungs, hilar adenopathy, and areas of pneumonitis are occasionally seen. Differentiation must be made from other fungous infections, brucellosis, malaria, tuberculosis, and diseases producing diarrhea, such as dysentery, idiopathic ulcerative colitis, and tuberculous enteritis.

Two of the authors' patients were infants and one was a 3-year-old child. In all the disease was of insidious onset. Symptoms and findings included intermittent fever, cough, anorexia, and lethargy, splenomegaly, hepatomegaly, and peripheral adenopathy. The fungus was found in bone marrow, blood smears, blood cultures, and node biopsies. Only 1 case showed x-ray findings, consisting of a triangular hilar density interpreted as pneumonitis or pleuritis.

All 3 patients died, since there is no effective treatment for the disease at present.

Five roentgenograms; 2 photomicrographs.

CORNELIUS COLANGELO, M.D.  
Chicago, Ill.

**Coccidioidomycosis. Review of the Literature and Report of Nine Cases.** Irwin L. Norman and Arthur L. Lawler. *U. S. Nav. M. Bull.* 49: 1005-1020, November-December 1949.

Nine cases of proved coccidioidomycosis seen during the past two years at the U. S. Naval Hospital, San Diego, are reported. Two patients with disseminated lesions died, and necropsies were done. In 3 cases the roentgen findings simulated lung tumor; in 1, unresolved pneumonia; in another, apical tuberculosis.

Seven roentgenograms; 2 photomicrographs.

**Infectious Mononucleosis, with Special Reference to Roentgenologic Manifestations.** James J. McCort. *Am. J. Roentgenol.* 62: 645-654, November 1949.

The author presents a rather complete historical survey of infectious mononucleosis and discusses the pathological changes described in the literature. These changes consist, in part, of marked proliferative activity within the lymph nodes with large numbers of atypical mononuclear cells and lymphocytes. Similar focal cellular infiltrates have been found in the lungs, liver, kidneys, heart, and other viscera.

During the past six years the diagnosis of infectious

mononucleosis has been made in 75 patients at the Massachusetts General Hospital. Forty-three had roentgen examinations of the chest. Six of this group and one other patient seen by the author showed changes which could have been attributed to infectious mononucleosis. These changes consisted of enlargement of mediastinal lymph nodes in 2 cases, mediastinal lymphadenopathy plus pulmonary parenchymal changes in 3 cases, and parenchymal changes only in 2 cases. There were no significant characteristic changes.

The diagnosis is not too difficult with a positive heterophile antibody test. However, the differential diagnosis roentgenographically must include all the diseases causing mediastinal lymphadenopathy, namely lymphoma, leukemia, sarcoid, tuberculosis, and others; and the parenchymal changes must be differentiated from atypical pneumonia and other virus infections.

Thirteen roentgenograms; 3 photomicrographs.

J. B. SCRUGGS, M.D.  
University of Arkansas

**Sarcoidosis: A Review of Eleven Cases Including Two Autopsies.** Ralph H. Nestmann. West Virginia M. J. 45: 240-246, September 1949.

Eleven cases of sarcoidosis are presented in table form. Only one of this series failed to show abnormal roentgenographic findings in the chest. In none of the cases were bone lesions found. The two autopsied cases are reported in greater detail. The pathologic diagnosis in one was "bilateral pulmonary non-caseating tuberculosis, identical with sarcoidosis associated with left apical pulmonary tuberculosis with cavitation." Death in this instance was attributed to tuberculosis. In the other case the pathologic diagnosis was "bilateral apical pulmonary scarring with bilateral lower lobe emphysema and bilateral pulmonary adhesions and sarcoidosis," and death was attributed to sarcoidosis involving the spleen, liver, and kidney.

The author points out that any case of pulmonary disease with radiologic evidence of enlarged hilar nodes, usual or unusual parenchymal shadows, and skin or eye lesions, should be investigated for sarcoidosis.

Three roentgenograms; 3 photomicrographs.

S. F. THOMAS, M.D.  
Palo Alto, Calif.

**Q Fever in a Veterans' Hospital.** R. W. Brawley and F. W. S. Modern. Arch. Int. Med. 84: 917-932, December 1949.

While roentgenograms of the chest play a small part in outright diagnosis of Q fever, radiologists should keep this "modern" disease in mind as a possible explanation of obscure chest findings. The present paper is chiefly concerned with the clinical observations in 12 cases.

Roentgenographically there is no characteristic finding. A patchy infiltration was present in 6 cases, a diffuse homogeneous density in 2, and a fine confluent infiltration in 1. The lower and middle lobes were more commonly involved. Robbins and Ragen (Am. J. Hyg. 44: 6, 1946. Abst. in Radiology 49: 114, 1947) found a predominance of lower lobe involvement. Regression of pulmonary infiltration in the authors' series occurred in twelve to sixteen days. In none of the series did the chest film obtained on discharge show completely normal findings. In 1 patient residual increased vascular markings were still present three months after discharge.

S. F. THOMAS, M.D.  
Palo Alto, Calif.

**Terminal Bronchiolar or "Alveolar Cell" Cancer of the Lung. A Report of Twenty Cases.** Robert R. Smith, Kenneth P. Knudtson, and William L. Watson. Cancer 2: 972-990, November 1949.

This report is based upon the study of 20 cases of terminal bronchiolar carcinoma found in reviewing all the cancers of the lung at Memorial Hospital (New York). Chest pain and cough were the most common presenting symptoms. Three cases were asymptomatic and were discovered on routine chest roentgenographic study.

Abnormal shadows were found in the chest roentgenogram in all 20 cases. The most common finding was a single, peripherally located, circular area of increased density, usually 2 to 4 cm. in diameter. Five patients showed multiple nodules, involving both lungs in several. The radiographic interpretation of malignant tumor was made in 65 per cent of the cases.

A clinical diagnosis of terminal bronchiolar carcinoma was made in 9 cases by means of thoracotomy, aspiration biopsy, or cytologic studies of the sputum. Cytologic studies of the sputum were done in 5 cases; 4 of these were recorded as showing conclusive proof of cancer and the remaining case was reported as suspicious of malignant tumor.

The treatment of terminal bronchiolar carcinoma is excisional surgery. Radiation therapy is a valuable adjunct in the palliative treatment of advanced cases. Nine patients in this series received definitive surgical therapy; 5 of these are living and 2 are well more than five years following excision of a solitary nodule of terminal bronchiolar carcinoma. Five patients received primary radiation therapy. Three had a hilar mass, 1 had diffuse disease throughout the lungs, and 1 had a mass and pleural effusion. All 5 patients died in four to eight weeks following the completion of therapy. A means of treatment which requires more study is the combination of surgery and irradiation, in which the primary bulk of the disease is excised and interstitial radon seeds are placed in the remaining inoperable cancer.

A discussion of the pathologic and histologic findings is presented. The relationship between this disease entity and so-called pulmonary adenomatosis, jaagsiekte, occupational and experimental lung cancer is discussed.

Six roentgenograms; 19 photomicrographs; 2 photographs; 6 tables.

DONALD S. CHILDS, JR., M.D.  
The Mayo Clinic

**Multinodular Carcinoma of the Lungs.** Josef Vaněk. Acta radiol. et cancerol. bohemoslov. 4: 97-119, 1949.

Primary carcinomas of the lungs are characterized by their great macroscopic multiformity as compared with malignant tumors of other organs. The rarest form is the multinodular (about 1 per cent). In this type no tumor changes are seen in the bronchi accessible to macroscopic examination, and to determine which nodule is primary is macroscopically and microscopically impossible. Schmincke has suggested what he designates as "holoblastosis," that is, a tumor change appearing simultaneously in the whole organ. Some authors denote the condition histologically as primary alveolar carcinoma, as distinguished from bronchogenic carcinoma.

The author describes a case, with autopsy, which

# Cancer of Robert R. L. Watson.

20 cases of  
viewing all  
pital (New  
ost common  
ymptomatic  
enographic

roentgeno-  
ading was a  
of increased  
of patients  
lungs in  
f malignant

r carcinoma  
y, aspiration  
Cytologic  
; 4 of these  
f cancer and  
us of malig-

arcinoma is  
valuable ad-  
anced cases.  
ive surgical  
l more than  
y nodule of  
patients re-  
had a bilar  
lungs, and 1  
patients died  
mpletion of  
quires more  
radiation, in  
excised and  
e remaining

ogic findings  
this disease  
ntosis, jaag-  
ing cancer is  
ographs; 2

Jr., M.D.  
ayo Clinic

ungs. Josef  
emoslov. 4:

acterized by  
mpared with  
arest form is  
n this type  
accessible to  
mine which  
icroscopically  
at he desig-

change ap-  
rgan. Some  
as primary  
ronchogenic

opsy, which

leads him to another conclusion than Schmincke's as to the origin of these tumors. The tumor in this case is described as a primary mucus-secreting cylindrocellular carcinoma which grew intra-alveolarly and spread equally in both lungs in the form of multiple nodules, no one of which could be said to be the primary lesion. The alveolar structure of the lung tissue in the tumors was without change and without signs of destruction. High cylindrical cells covered the alveoli in a single layer. The borders of the cells were sharp, and in some parts cilia were undoubtedly found. There were no metastases. Death was due to suffocation as a result of obstruction of the bronchial tubes by mucus.

The production of mucus and the occurrence of cilia lead the author to the conclusion that the tumor had its origin in the epithelium of the bronchi or bronchioli. He believes that it may not be a case of primary multiplicity but rather of dissemination from an undetermined primary focus, invasion occurring by the intra-bronchial route through aspiration, as was shown in a series of microscopic sections and by the fact that the tumor foci consisted often of a few alveoli only or even of a single alveolus, without any signs of spreading in the blood or lymph vessels in the surroundings. The invading tumor cells are implanted on the alveolar wall and progressively cover it.

The tumor then is a "special form of carcinoma originating from the bronchi or bronchioli in which intra-alveolar growth outweighs the ordinary growth by destruction and invasion, propagation occurring mostly by the bronchial route."

Two photomicrographs. CHARLES NICE, M.D.  
University of Minnesota

**Intrathoracic Pheochromocytoma with Hypertension.** Herbert C. Maier. *Ann. Surg.* 130: 1059-1065, December 1949.

A case of intrathoracic pheochromocytoma with hypertension is presented. Pheochromocytoma is usually found in or near the adrenals, and such cases are frequently accompanied by some type of elevated blood pressure. About 12 per cent of the cases, however, occur outside the adrenal area, and in these hypertension has only rarely been recorded. The extra-adrenal sites are chiefly near the kidneys or in the aortic bodies or organs of Zuckerkandl, which are located on either side of the aorta at the origin of the inferior mesenteric artery. Only two intrathoracic pheochromocytomas have been reported previously, both diagnosed at autopsy. The present case was diagnosed during life on the basis of an unexplained hypertension and the presence of an intrathoracic tumor in the region of the sympathetic chain in the costovertebral area.

A small number of pheochromocytomas are malignant, but in these cases there seems to be no hypertension.

Following surgical removal the blood pressure usually returns to normal.

Two roentgenograms; 1 photomicrograph.  
R. C. DATZMAN, M.D.  
Indiana University

**Solitary Intrathoracic Neurofibroma. A Report of Two Unusual Cases.** Arthur S. W. Touroff and Samuel O. Sapin. *Surgery* 26: 787-798, November 1949.

The majority of neurogenic intrathoracic tumors may be divided into two groups. Group 1 includes those

which arise from the nerve sheath. They may arise from spinal, cranial, or sympathetic nerves and are composed almost always of both neural and connective tissue. Group 2 consists of those which arise from the sympathetic nervous system. The incidence of malignancy in neurogenic tumors is significant, varying in frequency from 10 per cent to 37 per cent of cases reported in the literature.

The vast majority of intrathoracic neurogenic tumors arise from elements which lie within the posterior mediastinum. The authors report two cases of neurofibroma arising in unusual locations, both discovered during routine chest examination. In one case the tumor was situated in the right anterior axilla and was derived from the fourth intercostal nerve. Radiographically it appeared as an oval, sharply circumscribed density. There was no evidence of destruction of the adjacent ribs. The other patient had a lesion embedded in the apical portion of the right lower lobe. Films of the chest revealed a smooth, rounded, circumscribed density in the posterior mesial portion of the right hemithorax. There also was some vascular congestion of the right lung.

Seven roentgenograms.

HOWARD L. STEINBACH, M.D.  
University of California

**Pulmonary Effects of the Cocoanut Grove Fire. A Five-Year Follow-Up Study.** Helen S. Pittman and Richard Schatzki. *New England J. Med.* 241: 1008-1009, Dec. 22, 1949.

This is a follow-up study of the patients seen at the Massachusetts General Hospital following the Cocoanut Grove fire in November 1942 (Schatzki: *Ann. Surg.* 117: 841, 1943. *Abst. in Radiology* 42: 301, 1944). Of the 39 original patients, 16 have returned for examination; 6 have reported by mail; and 7 persons could not be traced. Three of the 6 reports received by mail were adequate; 2 patients had died, and the third was apparently psychotic.

Of the 16 who returned for examination, 15 were clinically well at the time of follow-up. The one exception was a 63-year-old man who had persistent râles in the right axilla.

Roentgen examination of the lungs of these 16 patients showed 13 to be normal. Two showed a single vertical line in the lower lung field representing either a linear scar or plate-like atelectasis. One of these had shown no abnormality on numerous examinations immediately following the fire. A third patient, not examined roentgenographically at the time of the disaster, showed a few similar lines in a basal segment of the right lower lobe.

Two patients reported the raising of copious amounts of sputum in the morning, and several had occasional dyspnea on effort. None reported persistent cough.

It would seem from this study that none of the patients suffered any permanent damage to the lungs that could be traced directly to the accident.

Two tables. JOHN B. McANENY, M.D.  
Johnstown, Penna.

**Medical Progress. Mediastinal Emphysema.** Mark Aisner and John E. Franco. *New England J. Med.* 241: 818-825, Nov. 24, 1949.

In this review of mediastinal emphysema under the general heading "Medical Progress," the author de-

votes a paragraph to the x-ray findings. He writes: "There seems to be little doubt that the diagnosis of mediastinal emphysema is often not suspected, and x-ray examination of the chest not made. On the other hand, the diagnosis, when suspected on clinical grounds, has not infrequently been ruled out on the basis of a single film taken in the postero-anterior projection. It should be emphasized that serial studies may be necessary, and that lateral views of the chest are essential, to demonstrate air trapped behind or in front of the heart. Air in the mediastinum is often visible as streaks of increased radiance running along the borders of the heart. The presence of air streaks along fascial planes and air pockets in subcutaneous tissue may be readily detected. Further aid, radiographically, may be furnished by demonstration of pneumoretroperitoneum and pneumoperitoneum. As mentioned previously, x-ray examination is invaluable in disclosing a small pneumothorax not manifest clinically."

**Ciliated Columnar Epithelial Cyst of the Mediastinum.** Victor O. Mader, Ralph P. Smith, and J. Avery Vaughan. *Canad. M. A. J.* 61: 525-528, November 1949.

The authors record a case of ciliated columnar epithelial cyst of the mediastinum which was successfully treated by surgery. They cite earlier reviews of the German and English literature and more recent reports, pointing out that their case brings the total number on record to 62. The symptoms that brought their patient under a physician's care were recurrent right pleurisy without effusion, non-productive cough, recurrent upper respiratory infections, weight loss, dyspnea on exertion, and a recurrent dull ache under the right breast. The cyst was demonstrated in roentgenograms, in the posterior mediastinum near the right hilus.

Diagnostic points to be noted fluoroscopically and radiographically are: (1) close relation of the cyst to the bifurcation of the trachea, seen best on the lateral films; (2) motion of the cyst when the patient swallows, since it is usually attached to the trachea; (3) absence of pulsation; (4) less dense shadow than teratoid tumors.

Two roentgenograms; 1 photomicrograph.

T. FREDERICK WEILAND, M.D.  
Jefferson Medical College

**Fibromyxoma of Pleura: Report of Case.** Edward W. Hauch and W. Walter Sittler. *Dis. of Chest* 16: 616-624, November 1949.

The authors give the case history of a 2-year-old girl with a fibromyxoma of the pleura. The child was brought to the hospital because of acute respiratory symptoms. Roentgen examination showed findings which were interpreted as a massive pleural effusion on the left side, displacing the mediastinum to the right, with partial atelectasis of the right lung. No fluid was obtained on thoracentesis. A diagnosis of an intrathoracic tumor was made because the trocar transmitted the sensation of probing solid tissue, but death ensued before thoracic exploration could be undertaken. Necropsy revealed a large fibromyxoma of the parietal mediastinal pleura (left side), bronchopneumonia, and atelectasis of the left lung.

These pleural tumors have three interesting features: they resemble pleural effusions; originate in various

portions of the pleura; and, though clinically they may appear benign, histologic examination indicates that they are malignant.

Data in 31 previously reported cases of giant tumor of the pleura are tabulated.

One roentgenogram; 1 photomicrograph; 2 tables.

HENRY K. TAYLOR, M.D.  
New York, N. Y.

**Selective Angiocardiography.** Gunnar Jönsson, Bror Brodén, and Johan Karnell. *Acta radiol.* 32: 486-497, Dec. 31, 1949.

Angiocardiography by injection of a contrast medium through the cubital vein is usually quite satisfactory in small children or in adults who show no abnormalities of the cardiac chambers or great vessels. When abnormal changes in the intrathoracic circulation exist, however, the dilution of the dye incident to its passage through the veins frequently prevents adequate visualization of the structures desired.

The authors illustrate and describe their technic of introducing the iodine solution directly into the cardiac chambers or great vessels through a No. 8 or 9 F catheter. This catheter is usually directed through the cubital or internal jugular vein. A catheter with as wide a bore as possible is recommended. Fifty to 70 c.c. of dye are injected with a pressure apparatus in three or four seconds. It is pointed out that too strong an injection of fluid from the catheter may cause extrasystole or even damage to the myocardium.

Serial films are made simultaneously in two planes at 90 degrees to each other. Better opacification of the left side of the heart and great vessels is accomplished by this method. No mention is made of harmful sequelae. The authors also recommend catheterization or cannulization of the arterial side of the circulation for angiocardiographic visualization of the aortic arch structures.

Twenty-one roentgenograms.

J. A. CAMPBELL, M.D.  
Indiana University

**Thoracic Aortography. Observations on Technical Problems Connected with the Method and Various Risks Involved in Its Use.** Bror Brodén, Gunnar Jönsson, and Johan Karnell. *Acta radiol.* 32: 498-508, Dec. 31, 1949.

Two methods for studying the thoracic aorta are recommended. One of these consists of the insertion of a cannula percutaneously into the common carotid artery, with subsequent threading of the cannula to the level of the anterior part of the aortic arch. The dye is then injected. The authors use this method for study of cases of coarctation of the aorta.

The second method consists of injection through a catheter inserted into the radial artery with the tip lying at the base of the aorta. Cases of patent ductus arteriosus are best shown by this method. Difficulties encountered are vascular spasm, difficulty in directing the catheter to the aorta, and difficulty in bringing the tip of the catheter into the correct position. Usually a No. 8 or 9 F catheter is used. Rapid injection is necessary.

In most of the authors' patients 50 c.c. of 70 per cent diodrast was injected, but because of the risk of cerebral complications, they now suggest using a 50 per cent solution.

Twelve roentgenograms; 1 drawing; 1 electrocardiogram.  
J. G. LORMAN, M.D.  
Indiana University

#### Angiocardiographic Diagnosis of Syphilitic Aortitis.

Israel Steinberg, Charles Dotter, George Peabody, George Reader, Leonard Heimoff, and Bruce Webster. *Am. J. Roentgenol.* **62**: 655-660, November 1949.

It has been estimated that 70 to 90 per cent of all patients with late syphilis detectable at postmortem examination show evidence of cardiovascular damage, usually syphilitic aortitis (Moore: *Modern Treatment of Syphilis*. Springfield, Ill., Charles C Thomas, 1944). The aortitis may be considered the fundamental cardiovascular lesion. Saccular aneurysm, aortic insufficiency, and coronary artery disease develop secondary to it.

The ideal management of cardiovascular syphilis is generally agreed to be its detection and treatment in the stage of uncomplicated aortitis. The application of specific therapy at this stage can be expected to result in arrest of the inflammatory process and prevention of more serious lesions.

The authors review the conventional methods of diagnosis, pointing out that roentgenography and roentgenoscopy of the chest have been of very considerable value in detecting cases of uncomplicated aortitis and differentiating them from other types of cardiovascular disease. Calcification of the ascending aorta has been found to be a relatively reliable sign of syphilitic aortitis; its presence, however, is not pathognomonic and its absence is of no diagnostic significance. Obvious widening of the aorta is significant but does not occur frequently enough to be used as a diagnostic criterion and is usually a late manifestation by the time it becomes evident on conventional roentgen examination. Moreover, the various measurements of aortic width have been shown to be indirect, inaccurate, and inapplicable to the root of the aorta, where the earliest manifestations of syphilitic aortitis occur.

Utilizing the angiocardiographic method of Robb and Steinberg, the authors found that in the presence of clinical or roentgen evidence of aortitis, and occasionally in their absence, certain angiocardiographic signs were regularly present. In 60 cases, the following signs were proved to occur most regularly: aortic dilatation, irregularity of the aortic lumen, calcification of the ascending aorta, aortic tortuosity, abnormal aortic wall thickness, and aneurysm.

Dilatation is the most significant angiocardiographic evidence of syphilitic aortitis. Measurements were made of dilatation in the left anterior oblique projection at four points: (1) the mid-ascending aorta, (2) the transverse aorta, (3) the mid-descending aorta, and (4) the diaphragmatic aorta. According to the authors the normal range for the mid-ascending aorta is from 16 to 38 mm. with an average of 28.6 mm., whereas in the presence of syphilis the range is from 38 to 70 mm., with an average of 45.4 mm. The ascending aorta is the earliest affected in syphilitic aortitis. It is concluded that in the presence of syphilis and in the absence of other detectable causes for aortic widening, dilatation of the aorta may be considered diagnostic of syphilitic aortitis. When syphilis is not present, observed dilatations of the ascending aorta may be due to hypertension, rheumatic aortic valvular insufficiency, or coarctation of the aorta. The authors have never observed aortic dilatation above the upper limit of

normal which could be attributed to arteriosclerosis alone.

In syphilitic aortitis the caliber of the aorta may seem to vary in a more irregular fashion than in non-syphilitic dilatation, a finding of definite differential value, observed in 95 per cent of the authors' cases. In their series roentgenographic evidence of calcification of the ascending aorta was present in 26.6 per cent of 66 proved cases of syphilitic aortitis.

One roentgenogram; 2 drawings; 1 table.

E. S. KERESKES, M.D.  
University of Arkansas

#### Calcification as a Diagnostic Sign of Syphilitic Aortitis. M. C. Thorner, R. A. Carter, and George C. Griffith. *Am. Heart J.* **38**: 641-653, November 1949.

Since calcific deposits in syphilitic aortitis are usually within the arch and ascending portions of the aorta, and the deposits in arteriosclerosis are usually in the descending portions of the thoracic and abdominal aorta, the roentgenographic demonstration of calcification in the various portions of the aorta should be of value in the differential diagnosis of these conditions.

The authors found calcification in the ascending aorta in 15 (39.4 per cent) of 38 unselected cases of syphilitic aortitis on roentgen study. Because of this, they reviewed all cases of syphilitic aortitis and atherosclerosis that came to autopsy within a given period. In 122 cases of syphilitic aortitis films were available, and 22 (18 per cent) showed calcification of the ascending aorta. Among 100 cases of atherosclerosis with roentgen studies, only 2 (2 per cent) showed calcification in the ascending aorta.

The average age of the syphilitic patients with calcification was 59.5 years (43 to 77); for those not showing calcification, 54.9 years (26 to 82). In the arteriosclerotic series the average age of the patients in whom calcification was present was 83 years (81 to 85); for those without calcification, 67.3 years (36 to 87). It is concluded that linear calcification of the ascending aorta in patients under sixty years is due to syphilitic aortitis in the majority of cases, and that, as pointed out by Jackman and Lubert (*Am. J. Roentgenol.* **53**: 432, 1945. *Abst. in Radiology* **46**: 310, 1946), this finding may outweigh the diagnostic implication of a negative serology.

The authors cite a case showing the presence of calcification of the ascending aorta in a patient with aortic stenosis and insufficiency thought to be rheumatic in origin, but proved to be syphilitic. Calcification of the ascending aorta is also of value in the differentiation of thoracic aneurysms from neoplasms. The demonstration of calcification, implying the presence of syphilis, may swing the balance in favor of aneurysm.

Eight roentgenograms; 2 photographs; 1 table.

HENRY K. TAYLOR, M.D.  
New York, N. Y.

#### Cardiac Enlargement in Uncomplicated Mitral Insufficiency in Children. Joseph H. Miller and Bernice G. Wedum. *Am. J. Dis. Child.* **78**: 703-707, November 1949.

The criteria for the diagnosis of mitral insufficiency, as set forth by the New York Heart Association, require the presence of enlargement of the heart in addition to a systolic murmur at the apex. Some clinicians state that the requirement of cardiac enlargement does

not apply to children or young adults. The authors report further evidence on this matter from observations on 1,971 children.

There were 82 children with a diagnosis of mitral insufficiency. Of these, 20 (24 per cent) showed enlargement of the left ventricle when examined by fluoroscopy in the anteroposterior and left anterior oblique positions. For controls, there were included 179 children with potential rheumatic heart disease. Three (1.6 per cent) of these showed enlargement of the left ventricle. One of 556 patients with clinically normal hearts showed enlargement of the left ventricle.

These observations support the conclusions that the diagnosis of mitral insufficiency can be made in the presence of the characteristic murmur and that cardiac enlargement need not necessarily be present.

One table.

DANIEL WILNER, M.D.  
Atlantic City, N. J.

**Criteria of Operability in Tricuspid Stenosis.** Henry Swan, George J. Maresh, and G. Robert Fisher. *J. Pediat.* 35: 604-610, November 1949.

The basic pattern of tricuspid stenosis is a diminutive or absent right ventricle combined with atresia or hypoplasia of both the pulmonary artery and tricuspid valve. In order to be compatible with life, this situation must be associated with an auricular septal defect and a ventricular septal defect or patent ductus arteriosus.

The diagnosis of tricuspid stenosis is based upon the roentgen demonstration of a small right ventricle and large left ventricle, the presence of left axis deviation on the electrocardiogram, and cyanosis. A cardiac catheter may be observed to pass into the left ventricle through a septal defect instead of into the right ventricle.

Surgery may be expected to be of benefit in those cases in which the blood reaches the lungs through a hypoplastic pulmonary artery and the pulmonary circulation is therefore diminished. The presence of a large patent ductus arteriosus and adequate pulmonary circulation is a contraindication to surgical interference.

The authors suggest, as a means of estimating the adequacy of the pulmonary blood flow, that the response of blood oxygen saturation to the inhalation of pure oxygen be determined. In those patients with diminished pulmonary circulation, there is no marked change in oxygen saturation of arterial blood and an aortic pulmonary shunt is indicated. In patients whose pulmonary circulation is good, a marked shift in arterial saturation may be expected. For these patients, operation is not indicated.

Two roentgenograms; 2 drawings; 1 table.

HOWARD L. STEINBACH, M.D.  
University of California

**Pulmonary Hemangioma with Pulmonary Artery-Aortic Septal Defect. Attempted Roentgen Visualization by Catheterization of Brachial Artery and Basilic Veins.** L. A. Erf, J. Foldes, F. V. Piccione, and F. B. Wagner, Jr. *Am. Heart J.* 38: 766-774, November 1949.

The authors give the history of a 20-year-old man in whom a diagnosis of pulmonary hemangioma (arteriovenous fistula) was made. A chest film revealed a dense oval shadow in the left upper lobe. Pulmonary arteriography and thoracic aortography with catheters failed to show contrast substance within

the pulmonary lesion. Following exertion, the patient collapsed as a result of a large pulmonary hemorrhage, and died. Postmortem examination revealed an hemangioma of the lung, right ventricular hypertrophy, and a large communication between the aorta and the pulmonary artery.

Details of 18 previously reported cases of pulmonary arteriovenous fistulas are tabulated.

Four roentgenograms; 1 photograph.

HENRY K. TAYLOR, M.D.  
New York, N. Y.

## THE DIGESTIVE SYSTEM

**Spontaneous Rupture of the Esophagus. Report of Two Cases: One with Recovery After Surgical Repair.** Eugene E. Clifton. *Ann. Surg.* 130: 1066-1073, December 1949.

Some 54 cases of spontaneous rupture of the esophagus have been reported, with 100 per cent mortality. The more recent cases are briefly reviewed and 2 additional cases seen at New Haven Hospital are presented. The first patient was a 35-year-old colored male who was alive nine months after operation. The second patient was a 75-year-old white male who died two and a half hours after the onset of his illness before a correct diagnosis could be made or surgery performed.

The history is usually typical, involving a bout of drinking or other over-indulgence followed by an attack of violent vomiting. The most valuable clinical sign is cervical interstitial emphysema in the presence of low substernal or epigastric pain. In many cases there will be signs of pneumothorax, hydrothorax, or both. The standard roentgenogram of the chest may show mediastinal gas shadows, sometimes with fluid levels. A definite diagnosis may be made by demonstrating extravasation of a swallow of lipiodol into the mediastinum or pleural cavity.

Surgery is the only treatment, though the author's first case is the only one reported with satisfactory response.

Three roentgenograms.

J. S. SCOTT, M.D.  
Indiana University

**Periesophageal Thickening Following Ingestion of Lye.** E. Fracasso and G. Gurian. *Radiol. med. (Milan)* 35: 877-885, November 1949. (In Italian)

The authors studied 12 patients in whom, following ingestion of lye, there was marked thickening of the periesophageal tissues along with the usual deformities of the lumen. This thickening was seen especially well in the oblique and lateral positions and usually involved the middle and lower thirds of the esophagus. The barium inside and the transparent mediastinal and lung tissues on the outside provided the necessary contrast.

The authors stress the importance of observing the soft periesophageal shadows for more accurate diagnosis, not only in inflammatory reactions, but also to show the extent of neoplastic invasion.

Nine roentgenograms. CESARE GIANTURCO, M.D.  
Urbana, Ill.

**Some Limitations of Vagotomy in the Treatment of Peptic Ulcer: A Critical Follow-up Analysis of Fifty Cases.** Martin J. Healy, Jr., and Paul K. Sauer. *Ann. Surg.* 130: 985-1007, December 1949.

The authors present an interim analysis of 50 cases of

the patient  
hemorrhage,  
aled an he-  
rtrophy, and  
the pul-

pulmonary

OR, M.D.  
rk, N. Y.

Report of  
urgical Re-  
130: 1066-

the esoph-  
mortality.  
and 2 addi-  
presented.  
male who  
The second  
two and a  
e a correct

y a bout of  
by an at-  
ole clinical  
presence of  
cases there  
e, or both.  
may show  
uid levels.  
onstrating  
the medi-

e author's  
atisfactory

r, M.D.  
iversity

gestion of  
iol. med.  
alian)

following  
ng of the  
eformities  
especially  
usually in-  
sophagus.  
tinal and  
sary con-

erving the  
diagnosis,  
show the

M.D.  
na, Ill.

tment of  
of Fifty  
Sauer.

cases of

intractable, non-obstructing duodenal and marginal ulcer treated by transthoracic vagotomy, in an attempt to determine the long-term effect of the procedure.

The criteria for selection of cases for vagotomy were: (1) symptoms of intractable pain, chronic bleeding, or both; (2) failure to control symptoms by adequate medical regimen; (3) evidence of active ulcer by roentgen ray; (4) no retention, clinically or by roentgen ray.

The patients received a standard preoperative work-up, including histamine gastric analysis, overnight secretion studies, insulin tests, and roentgen examination. These procedures were repeated early postoperatively and on one or more follow-up examinations.

The immediate postoperative results were relief of pain in all but 2 cases and reduction in overnight secretion and free hydrochloric acid levels. The complications were pleural effusion in 40 per cent, and in 80 per cent varying degrees of fullness in the epigastrium, belching, pyrosis, regurgitation, and vomiting. In 5 patients such severe atony developed early in the post-operative period that gastric resection or gastroenterostomy was performed.

The follow-up period averaged only eighteen months, but pain had been noted to recur or persist to some extent in 56 per cent of the cases. Seven of 32 patients reported bleeding preoperatively and 2 others reported bleeding after vagotomy. The roentgen examinations showed active ulcers in roughly 2 out of 5 cases. Tonus was regained in the majority but 36 per cent had definite atony and gastric retention seven to twenty-seven months after surgery. Persistent diarrhea was not an outstanding complaint.

Considering the entire series, only 46 per cent escaped severe or prolonged symptoms attributable to nerve section. The overnight secretion and free hydrochloric acid were found to increase during the follow-up period.

Brief protocols of all 17 cases classified as failures are given. Five of these cases required surgery within three months and in 4 additional ones operation was done after six to twenty-seven months.

The authors believe that the relatively large percentage of unsatisfactory results indicates that vagotomy alone has serious limitations in the treatment of peptic ulcers. Despite the low mortality, failures are too frequent and morbidity too serious after vagotomy to justify its substitution for other proved methods of surgical treatment.

Seven roentgenograms; 3 tables.

DAVID C. GASTINEAU, M.D.  
Indiana University

**Hourglass Stomach Caused by Annular Muscular Hypertrophy. Report of a Case.** C. Morrison Schroeder. *Ann. Surg.* 130: 1085-1090, December 1949.

A 79-year-old male presented himself at the hospital with pain in the epigastrium of one month duration. An epigastric mass was palpated, and x-ray study of the stomach revealed a typical hourglass deformity of the antrum. The preoperative diagnosis was gastric carcinoma. At operation the constriction was found to be 3 cm. thick. The pathologic report was "annular constriction due to muscular hypertrophy."

Two excellent illustrations of the x-ray findings, a photograph of the operative specimen, and a photomicrograph are included. JAMES G. LORMAN, M.D.  
Indiana University

**Phytobezoar in the Gastric Stump. Report of a Case and Discussion of Therapy.** L. Walk. *Arch. Int. Med.* 84: 824-835, November 1949.

A case is presented of a phytobezoar in the stump of a stomach which had been partially resected for suspected cancer. The phytobezoar apparently was not detected by roentgen examination five days before its discovery, at which time it measured 5 × 6 × 7.5 cm. on the films. Subsequent roentgen examination showed it to be decreasing in size, and after forty-five days it was no longer demonstrated.

The author states that phytobezoars frequently disappear spontaneously and should be followed for a period of four weeks, if no complications are present, before surgery is resorted to. However, in stomachs which have artificial anastomoses, surgery is indicated because of the frequent occurrence of obstruction of the jejunum. If obstruction occurs in patients who have had no anastomoses, it usually is in the ileum.

Gastric ulcers associated with phytobezoars usually heal after disappearance or removal of the foreign body. Three roentgenograms; 4 tables.

HOWARD L. STEINBACH, M.D.  
University of California

**Cholecystocolic Fistula. A Review and Case Report.** James F. Crenshaw. *South. M. J.* 42: 935-943, November 1949.

The author reviews the literature on spontaneous internal biliary fistulae and then discusses the causes, diagnosis, prognosis, and treatment of one particular type, the cholecystocolic fistula. Finally he reports a case in which a roentgen diagnosis was made.

Most cholecystocolic fistulae are complications of chronic calculous cholecystitis. Other rarer causes are carcinoma of the gallbladder, acute cholecystitis, and empyema of the gallbladder. The clinical diagnosis is not easy but would probably be made more often if certain suggestive symptoms were borne in mind. Occurrence of acute diarrhea or sudden relief of symptoms of biliary tract disease suggests the development of a fistula between the gallbladder and gastro-intestinal tract. Passage in feces of biliary stones too large to pass the ampulla of Vater is obviously of significance.

Roentgen diagnosis of cholecystocolic fistula is based upon (1) barium stream connecting the gallbladder (or bile ducts) with the large bowel; (2) gas influx into the biliary system from the colon; (3) non-visualization of the gallbladder in the cholecystogram; (4) mucosal changes in colon at the site of the fistula; (5) inference, from biliary calculus in the bowel.

The treatment of choice in cholecystocolic fistula is surgery, though surgical repair has been attended by a mortality rate of 50 to 60 per cent in the past.

In the case reported, a roentgen diagnosis was made preoperatively by visualization of gas connecting the colon and biliary system. The biliary tract and the fistula were outlined by barium during the course of a barium enema study. Surgical repair was successful.

Four roentgenograms; 1 drawing.

T. FREDERICK WEILAND, M.D.  
Jefferson Medical College

**Diaphragmatic Hernia with Complete Evisceration of the Liver.** W. P. Kleitsch, A. D. Munger, and W. F. Johnson. *Ann. Surg.* 130: 1079-1084, December 1949.

A case of total evisceration of the liver and gallbladder through the diaphragm is presented as the only

such case in an adult to be found in the literature. The patient, a 54-year-old male, had urinary signs and symptoms and gave a history of having sustained fractures of several ribs, the left patella, and the pelvis six and a half years previously. He was left with a speech defect and a right hemiplegia by this violent trauma.

On the current admission a chest roentgenogram showed an elevated right diaphragm with pleural reaction above it. A right renal calculus was surgically removed. Postoperatively dyspnea, cyanosis, and abdominal distention developed. Roentgenograms showed the gas-filled colon in the right thorax and no liver shadow in the abdomen. Subsequent thoracotomy revealed a central circular defect in the right diaphragm 10 cm. in diameter. Protruding through it and filling the right thoracic cavity were the entire liver, gallbladder, transverse colon, and hepatic flexure. The abdominal viscera were returned to the abdomen by enlarging the defect, which was successfully closed. The patient recovered, with no recurrence of the hernia.

The etiology of the hernia and evisceration could not be definitely classified as congenital or traumatic. In view of the history, the latter seemed possible. Either origin left questions unanswered. It is noted that the evisceration was missed on a preoperative roentgenogram and that such evisceration is symptomatic only when the gastro-intestinal tract becomes involved, as was the case here when postoperative ileus had produced marked distention.

The importance of a careful study of all roentgenograms is re-emphasized. If, as in this case, attention is directed exclusively at obvious pathologic lesions, associated conditions will often be overlooked. The judicious use of bedside roentgenography in the postoperative period is also stressed.

Three roentgenograms; 1 drawing.

D. E. VIVIAN, M.D.  
Indiana University

### THE MUSCULOSKELETAL SYSTEM

**Orthopedic X-ray Problems in Children.** G. Newton Scatchard. New York State J. Med. 49: 2545-2547, Nov. 1, 1949.

The author stresses certain rules that must be followed in order to evaluate properly and understand x-ray findings in the bony structures in children. Comparative films should always be taken when possible. If there is any doubt as to the extent of the examination, it is best to err on the side of studying too many parts too thoroughly. Those anatomic regions which most commonly are puzzling have been selected for this paper.

The criteria for the diagnosis of congenital dislocation of the hips in young infants are as follows: When the angle of the roof of the acetabulum measures over 30 degrees in an infant over six weeks of age, it is considered a potential dislocation. Another indication of dislocation is the relationship of the femoral head to a line erected perpendicular to another line drawn through the inferior medial edge of the roof of the acetabula. The perpendicular is erected from the upper outer corner of the acetabulum. Normally the femoral head lies medial to the perpendicular line, while the dislocated hip lies with its head lateral to the line. Also, the dislocated hip usually lies above the base line. Still another indication is the size of the upper femoral epiphysis.

When ossified, this is invariably smaller on the side of the dislocation.

Osteomyelitis of the femoral neck may cause a dislocated hip in a young infant and lead to a mistaken diagnosis of congenital dislocation. The differential features are as follows: In the first place, the roof of the acetabulum is normal, and the hip is painful. The second point is a fullness of the soft tissues around the hip joint. Such a hip will automatically slip back into place following aspiration of the pus.

In older children, the point of fusion of the ischium with the symphysis may be erroneously diagnosed as fracture, bone cyst, bone tumor, and exostosis.

Perthes' disease, slipped femoral epiphysis, and tuberculosis of the hip joint may be confused but are usually rather easy to differentiate. Perthes' disease shows flattening of the upper femoral epiphysis, with increased density, widening of the joint space, and a translucent area in the upper portion of the femoral neck adjacent to the epiphyseal line. This usually occurs in children under the age of ten years. Slipped femoral epiphysis occurs in older children. The density of the head remains normal, and the slipping is obvious if both anteroposterior and lateral views are taken. The age range is usually between twelve and fourteen years. Tuberculosis of the hip can occur in any age group. There are narrowing of the joint space, bone atrophy, and destruction.

The wrist joint rarely causes serious diagnostic problems in children. Greenstick fractures are common and readily diagnosed. The evaluation of damage at the epiphyseal line is somewhat more difficult and impossible without comparative films.

The elbow joint is one of the most difficult areas for evaluation of injury. The medial epicondyle is the most frequent site of injury and comparative films are most important in this situation. Greenstick fractures in the supracondylar region as well as epiphyseal injuries to the head of the radius also fall in the same category.

The knee joint causes difficulty much less often than the elbow joint. An early case of osteochondritis dissecans may be diagnosed when utilizing comparative film technic.

The clavicles and shoulders in young infants are frequently difficult to visualize well. Fractures of the medial end of the clavicles are often missed. A rare but important lesion of the shoulder is the Codman tumor, which in its early stages has the radiographic appearance of an osteomyelitis and later comes to look like a malignant bone tumor, usually an osteogenic sarcoma. These tumors respond well to x-ray therapy or curettage and should certainly be kept in mind.

The author emphasizes that trauma in young infants and children is very common, even without a history of injury. X-ray studies of children because of a slight limp or a questionable swelling will often uncover an unsuspected fracture.

DANIEL WILNER, M.D.  
Atlantic City, N. J.

**Mandibular Growth Disturbance in Rheumatoid Arthritis of Childhood.** Milton B. Engel, Julius Richmond, and Allan G. Brodie. Am. J. Dis. Child. 75: 728-743, November 1949.

Six children manifesting mandibular involvement during the course of rheumatoid arthritis were studied by the author. Roentgenographically the mandible was shown to be deformed and to have failed to attain its full growth potential. The height of the ramus was re-

duced and the body shortened. Measurement of the angular relation between the mandible and the rest of the craniofacial complex emphasized this. Laminagrams of the temporomandibular joint showed the changes more clearly. The condyles were flattened and stunted, and in early stages one could see evidence of erosion. The temporal surface of the joint suffered loss of contour and was flattened. Frequently there was a haziness about the area of the joint which was associated with periarticular fibrosis.

The authors feel that since the condylar area is an important growth site, it may be injured by the inflammatory reaction in rheumatoid arthritis. Furthermore, growth of the mandible may become definitely decelerated because of an inhibitory effect of the arthritic process on proliferation of cartilage and ossification. The continued growth of the soft structures of the floor of the mouth, particularly the tongue, associated with the retarded forward and downward movement of the mandible, frequently results in encroachment on the pharyngeal space. The pathogenesis of the facial deformity and disturbed relationship of the jaws and dental arches is discussed.

Ten roentgenograms; 3 photographs; 1 drawing; 1 photomicrograph.  
DANIEL WILNER, M.D.  
Atlantic City, N. J.

**Fibrous Dysplasia of Bone.** James N. Proffitt, Barton McSwain, and Edmond H. Kalmon, Jr. *Ann. Surg.* 130: 881-895, November 1949.

The authors present the clinical, laboratory, roentgenologic, operative, and pathologic manifestations of 7 cases of fibrous dysplasia of bone, with follow-up studies on 6. Some of the many terms which have been applied to this disease are Albright's syndrome, polyostotic fibrous dysplasia, osteodystrophia fibrosa, localized von Recklinghausen's disease, osteitis fibrosa disseminata, and regional fibrocystic disease. As seen on the roentgenogram, the bone lesions were usually irregular areas of rarefaction which varied greatly in size and shape. In one case there were several small areas measuring only 3 or 4 mm. in diameter, whereas in another case the pathologic process involved almost the entire length of the tenth rib. The "ground-glass" appearance of the rarefied areas usually led the roentgenologists to believe that the lesions were cystic. With one exception, bony trabeculae were seen projecting into the areas of increased penetration. Generally, there was expansion of the bone with thinning of the cortex in all lesions over 5 mm. in diameter. One case showed disruption of the cortex of a rib, and in 3 patients bone of increased density was seen around the margins of the areas of decreased density. In each of 3 patients the lesion was single, in 1 patient there were multiple lesions in a single bone, and in 3 individuals there was involvement of multiple bones. There was no instance of generalized bone decalcification such as is seen in hyperparathyroidism.

Fractures were seen in 4 patients, 1 having had fractures of three bones.

In the single patient in whom the skull was involved, the bones near its base showed dense sclerosis and thickening.

A tentative diagnosis of fibrous dysplasia of bone should be made if the bone involvement is multiple and predominantly unilateral.

A surgeon who has not previously seen this syndrome usually expects to find at operation a cavity containing

fluid. In all of the 7 patients, however, exploration of the bone revealed solid tissue, and in only 1 of them was there any tissue which was not solid.

Upon microscopic examination alone, one can positively differentiate fibrous dysplasia from giant-cell tumor, but not from solitary bone cyst or osteitis fibrosa cystica. The two constant findings are connective tissue and osteoid tissue, i.e., young bone which has not been calcified. The areas of new bone formation ranged from acidophilic osteoid tissue to adult calcified bone. In only one instance were giant cells seen, and these were readily distinguishable from those seen in giant-cell tumor by the fact that their nuclei ranged from 2 to 10 in number instead of from 15 to 200.

The clinical and roentgenologic manifestations of fibrous dysplasia in a single site and those of solitary bone cyst are almost identical, and microscopic examination of the material from lesions of fibrous dysplasia reveals findings quite similar to those seen in the lining of a bone cyst. Since in both diseases healing often occurs following spontaneous fracture or curettage, it is not extremely important to distinguish between these lesions. However, it is necessary to differentiate fibrous dysplasia in its polyostotic form from osteitis fibrosa cystica, to prevent the patient being subjected to a search for a parathyroid adenoma. In 3 of the 7 cases being reported, neck exploration was done, with death upon the operating table in 1. No parathyroid tumor was found in any of the 3 patients. Normal phosphorus levels and calcium levels which are normal or only slightly elevated, plus the operative finding of solid tissue in the bone instead of fluid, are nearly always adequate criteria upon which to make this differentiation. With equivocal findings it may be necessary to demonstrate the absence of negative calcium balance in order positively to rule out the presence of hyperparathyroidism.

The follow-up studies indicate that the lesions of fibrous dysplasia of bone may remain unchanged for many months or even years and that healing occurs following removal of the fibrous tissue.

Fifteen roentgenograms; 2 photomicrographs; 3 photographs; 5 tables.  
DANIEL WILNER, M.D.  
Atlantic City, N. J.

**Fibrous Dysplasia of a Rib.** Nicolás N. Perruelo and Pablo Rossi. *Prensa méd. argent.* 36: 2345-2349, Nov. 11, 1949. (In Spanish)

The publication of this case was stimulated by the diagnostic difficulties presented and by the anatomic and pathologic proof which was later obtained. The patient was a 28-year-old man who about a year before began to suffer pain in the right chest at the level of the sixth rib anteriorly. The pain, although periodic, was persistent, and finally disability was such that operation was done.

The x-ray findings indicated a clean-cut lesion, with smooth, regular, and thin borders. The interior of the cyst-like structures presented a homogeneous opaque field divided into various compartments of short diameter (multilocular). There was no bony reaction in the vicinity of the periphery or in the periosteum or surrounding soft tissues. No other similar lesions were found.

Under local anesthesia a piece of rib was removed, presenting a tumefaction the size of a nut, causing a fusiform enlargement of the bone, mostly on its internal surface. The microscopic evidence indicated fibrous

dysplasia of the rib. The lesion was of slow, torpid evolution.

In the differential diagnosis the following were considered and excluded: giant-cell tumor, tertiary syphilitic gumma, chondroma, hydatid cyst.

Five illustrations.

JAMES T. CASE, M.D.  
Chicago, Ill.

**Polyostotic Fibrous Dysplasia.** Louis J. Hackett, Jr., and William M. Christopherson. *J. Pediat.* 35: 767-771, December 1949.

A case of polyostotic fibrous dysplasia in a 5-year-old white female is presented. It is unusual in that menstruation began on the second day of life and continued regularly at twenty-eight-day intervals. Other signs of precocious sexuality were present. Several areas of dark brown pigmentation were present over the right side of the trunk, abdomen, and buttocks. Laboratory studies were normal. Roentgen examination revealed multiple areas of "cyst-like" lesions involving the humerus, ulna, metacarpals, phalanges, ilium, femur, tibia, and fibula on the left side, and femur and fibula on the right side. There was a pathological fracture of the middle third of the left tibia. The diagnosis was confirmed by a biopsy of the left fibula.

Four illustrations, including 1 roentgenogram.

HOWARD L. STEINBACH, M.D.  
University of California

**Cranio-Cleido-Dysostosis.** H. A. Thomas Fairbank. *J. Bone & Joint Surg.* 31-B: 608-617, November 1949.

Cranio-cleido-dysostosis is a congenital disease of unknown etiology, but with a hereditary factor, characterized chiefly by deficient formation of the clavicles and delayed and imperfect ossification of the cranium. The sexes are about equally affected. Although present at birth, the defects may not be discovered for years, due to the relative lack of symptoms. The author gives a complete account of the findings in this disease together with 5 case reports which are well illustrated.

In cranio-cleido-dysostosis, growth as a whole is retarded, and there may be dwarfism. More usually, however, the patient is of slender build, with a long neck surmounted by a large head which is due to bossing of the frontal, occipital, and parietal bones. There may be some hydrocephalus. The base of the skull is ossified normally, but the calvarium is imperfectly ossified, resulting in an open anterior fontanelle and failure of closure of the sutures. In an extreme case there may be no ossification of the vault. The skull defects appear to be always symmetrical.

The clavicular error is present almost without exception. This may vary from complete absence of both clavicles to absence of one of the ends of a single clavicle, the outer end more commonly. The defects are usually easily felt, although sometimes there may be no more than a kink in the middle of the bone or a dimple of the skin. Weakness of the shoulders is the most common result, and there may be subluxation of the humeral head, dislocation, winged scapulae, or small deformed scapulae. The deformity of the clavicle may be complicated by pressure on the brachial plexus, which can be relieved by surgery.

The defects associated with this disease may also occur in bones preformed in cartilage. Thus the pubes may show deficient ossification, but this is not obvious clinically. Radiographic demonstration of abnormal

ossification of the pubes is good evidence for the disease.

The neural arches commonly fail to fuse, and there may be other anomalies, such as hemivertebra and bi-convex vertebral bodies; syringomyelia may be present as a complication.

In the author's series of 11 cases, there were 5 with coxa vara, which was of the infantile or cervical variety. Others have reported varus deformity of the upper part of the femoral shaft, deformity of the acetabula, and increased mobility of the hip joints.

There is considerable variation in the distribution and form of the abnormalities, such as the presence of epiphyses at both ends of the metacarpals and metatarsals, poorly developed ungual tuberosities, short calcaneum, delay in ossification of the carpus, delayed eruption, non-eruption, and incomplete development of the teeth, prognathous mandible, supernumerary permanent teeth, dentigerous cysts, etc.

Sixteen illustrations, including 13 roentgenograms.

GABRIEL WHITEMAN, M.D.  
Louisville, Ky.

**Achondroplasia.** Synonyms: **Chondrodystrophia foetalis, Micromelia.** H. A. Thomas Fairbank. *J. Bone & Joint Surg.* 31-B: 600-607, November 1949.

Achondroplasia is a congenital condition of unknown etiology which results from interference with endochondral ossification. It is the commonest type of dwarfism. Females are affected slightly more frequently than males. Although the disease is hereditary, 90 per cent of cases are sporadic, due to the interference with inheritance caused by difficult labor in the achondroplastic female. The abnormal endochondral ossification is apparent toward the end of the second month of fetal life. Birth is often premature, at about the eighth month, and 80 per cent of affected infants die during the first year of life, usually at or soon after birth.

The dwarfism affects mainly the proximal long bones. The spine may show kyphosis, or lordosis, which is often more apparent than real, due to the prominence of the buttocks. The head is large, being especially prominent in the frontal region, and brachycephalic. There may be some hydrocephalus. The lips are thick, and the tongue may protrude, but the dentition is normal. The chest is small and flat, due to the abnormal shortness of the ribs, and in extreme cases death may be due to inadequate capacity of the thorax. The shoulders are of normal breadth, but movements of the shoulder joints and supination of the forearms may be somewhat limited. The hands are broad and short; the fingers are all of almost equal length and appear to diverge (*main en trident*). The legs may be bowed due to curvature of the tibiae. The gait is rolling as a result of the backward tilt of the pelvis and posterior displacement of the hip joints. Occasionally, the dwarfism may be localized to one limb.

Radiographically, the long bones are short and dense. The shafts may be actually thickened, and there may be reduction in size of the medullary canal by cancellous bone. There is seen rather abrupt splaying of the ends of the shafts, and in some of the bones the end of the shaft is notched centrally, with the epiphyseal center tucked into the apex of the V-shaped notch. This results in an apparent increase in width of the joint space. The scapula and pelvis present a characteristic appearance; the scapula appears to have had

its inferior angle cut off; the ilium is small and is of a curious shape. The vault of the skull is large, but the base of the skull is diminished in length; the foramen magnum may be so reduced in size as to result in death of the patient. The clavicles and fibulae are less affected than other long bones. The facial bones are entirely unaffected.

The pathological picture is one of disordered growth of the cartilage cells of the epiphyses, with poor provisional calcification. Endochondral ossification is irregular, but periosteal ossification is normal or excessive.

Achondroplasia must be differentiated from chondro-osteodystrophy, gargoylism, cretinism, osteogenesis imperfecta, and dysplasia epiphysealis punctata.

Fifteen illustrations, including 11 roentgenograms.

GABRIEL WHITEMAN, M.D.  
Louisville, Ky.

**Osteitis Tuberculosa Multiplex Cystica: Its Treatment with Streptomycin and Promizole.** Martin Turkish, James W. Murphy, Peter Roody, and Raymond Saigh. *J. Pediat.* 35: 625-629, November 1949.

Osteitis tuberculosa multiplex cystica in children has the following characteristics: (1) The onset is gradual, usually during puberty or thereafter. (2) Pain is present early but is not severe. (3) The small long bones of the hands and feet, and sometimes the long hollow bones, are involved. (4) There is marked cystic degeneration of bone, with a tendency of the smaller lesions to fuse and form large cysts. (5) There is no involvement of the periosteum or joint. (6) Tuberculin tests, guinea-pig inoculations, and cultures frequently are positive. (7) Although the local lesions have a tendency to heal, death frequently occurs as a result of generalized tuberculosis.

The case of a 19-month-old Negro infant is reported. The child had an abscess on the dorsum of the right hand. Roentgen examination showed a notch-like defect at the junction of the distal and middle thirds of the right third metacarpal. The medullary canal was widened and the cortex was thinned, with a fine, subperiosteal laminated bone formation being present. Numerous punched-out areas were scattered through the parietal and frontal bones of the skull. Several large, cyst-like, sharply outlined, rather ragged areas of bone rarefaction were demonstrable in the right horizontal ramus and mental region of the mandible.

Two months after streptomycin and promizole treatment was begun, the metacarpal lesion had healed. The skull and mandibular lesions healed after five or six months.

This is the eighteenth proved case in the literature. It is the first reported case that has been treated with streptomycin and promizole.

Three roentgenograms.

HOWARD L. STEINBACH, M.D.  
University of California

**Osteitis Pubis: A Urologic and Roentgenographic Study.** Edward W. Beach. *Urol. & Cutan. Rev.* 53: 577-584, October 1949.

This study is based upon 7 cases of osteitis pubis seen in the author's private practice in three years. Four of these cases followed suprapubic prostatectomy, 2 bladder resection, and 1 transurethral resection. Biopsy was done in two cases and the bone changes are interpreted as a panosteitis.

The author considers osteitis pubis the result of the spill of urine or septic material into the deep pelvis, incident to urologic surgery. Because of the inherent pelvic fascial arrangement, such material will collect initially behind the pubic bodies and, unless adequately drained, will extend beneath the arcuate tendons and into the ischial region. The incidence of osteitis pubis is thus conditioned upon trauma, septic spill, and inadequate drainage.

On the eighth to the twelfth postoperative day the patient complains of vague pain in the groin and low back region and some stiffness in the muscles on the medial side of the thighs. Soon all movements of the legs are painful, the legs can be crossed only with great difficulty, and cannot be separated widely. The patient is usually unable to stand or sit comfortably. In the early stages he also complains of pain on micturition and defecation, evidently due to spasm of the levator ani muscles. Pressure over the symphysis pubis also elicits pain. The recti muscles are tense and guarded and the adductor group of thigh muscles are spastic.

Roentgenologically, peculiar rounded, oval, or crescent-shaped areas of reduced density or osteoporosis appear simultaneously in both pubic bones. These areas, which indicate resorption of the mineral salts, have a moth-eaten, irregular appearance, with fuzzy margins. This process represents acute bone atrophy. There was never any tendency to cyst formation or sequestration in the author's cases. No gross periosteal change could be detected in the early stages, but later some fraying usually appeared. Osteoclastic changes predominated in the first four to six weeks, at the end of which time osteosclerosis began at the margins, progressing in orderly fashion and "with crescendo." The bone changes, both rarefactive and osteoblastic, could be detected in the pubic bone as long as twenty-eight months after the initial process, despite absence of symptoms. Clinical progress corresponded fairly closely to the reparative changes in the bone noted roentgenologically.

With this malady an ounce of prevention is worth a pound of cure. The disease is self-limited, but recovery is conditioned by the severity of the symptoms and the extent of osseous change. The average recovery time in the author's series of 7 was three and a half months.

Fourteen roentgenograms.

HUGH A. O'NEILL, M.D.  
Cleveland, Ohio

**Multiple Myeloma with New Bone Formation.** Philip Krainin, Carl J. D'Angio, and Ammiel Smelin. *Arch. Int. Med.* 84: 976-982, December 1949.

This report of a case of multiple myeloma describes a bizarre finding in a disease whose pathological manifestations in bone are generally accepted as a discrete osteolytic involvement. In this patient there was proliferative new bone formation involving the entire shaft of the humerus, clearly shown in the reproduction of the roentgenogram. Review of a large number of autopsy protocols brought to light no reports of new bone formation of significant degree in multiple myeloma other than at the site of a pathological fracture, and no mention of this finding was discovered in the literature.

[The abstracter has seen 3 cases where new bone formation took place in myeloma: 1 case spontaneously while the patient was under medical care, a second case following x-ray therapy, and a third case in erythroblastic myeloma.]

Six illustrations including roentgenograms and photomicrographs demonstrating the bone proliferation.

S. F. THOMAS, M.D.  
Palo Alto, Calif.

**Roentgen Diagnosis of Osteoporosis, in the Concentration Camp at Theresienstadt.** Lilly Pokorná. *Radiol. clin.* 18: 360-370, November 1949. (In German)

This article is based on observations made at the concentration camp at Theresienstadt from March 1942 to July 1945. The average age of the prisoners was sixty-seven and a half years. Osteoporosis was observed mainly in the thorax, spine, and pelvis. Changes in structure and form of the bones are described.

The osteoporosis of the bony structures of the thorax and of the vertebrae was found to be identical with the usual findings. The pelvis, however, showed interesting changes in addition to the generalized osteoporosis: a marked flattening due to reduction of the conjugata vera and insufficiency fractures of the rami of the pubic bones.

These changes varied with the age and nutritional status of the prisoners.

Five roentgenograms.

EUGENE F. LUTTERBECK, M.D.  
Cook County Hospital, Chicago

**The Effect of Intramedullary Nailing on the Healing of Fractures. An Experimental Study.** William T. Fitts, Jr., Brooke Roberts, Stanley I. Spont, and Vern W. Ritter. *Surg., Gynec. & Obst.* 89: 609-615, November 1949.

Roentgen studies were made of experimentally fractured ulnas in 14 dogs. The fractures were bilateral. On one side a stainless steel Kirschner wire, 1.2 mm. in diameter, was inserted through the olecranon process into the medullary cavity and past the fracture site into the distal fragment. The opposite bone served as a control. In every instance extensive periosteal callus at a distance from the fracture site was noted on the pinned site. That the reaction was not due to infection was indicated by freedom from clinical signs of infection and absence of infection when the dogs were later sacrificed. Boehler has attributed some types of periosteal callus ("periosteal appositions") to rusting of the nail. In these experiments no instance of rusting of wire occurred. The periosteal reaction reached its peak roentgenologically at about four to six weeks after pinning and then gradually disappeared.

In 2 additional dogs in which Steinman pins were inserted into unfractured femurs, the periosteal reaction was found only opposite the points where the pin was in direct contact with the inner side of the cortex.

The pinned fractures healed more rapidly than those on the opposite side, but this is believed to be due to immobilization rather than to a callus-stimulating effect. Distraction was shown to exert a definite deleterious effect on fracture healing.

Twenty-one roentgenograms; 1 photomicrograph; 1 table.

**Resorption of Abrodil in Myelography.** Torfinn Denstad. *Acta radiol.* 32: 428-434, Dec. 31, 1949.

Lindblom, in a review of 721 cases in which abrodil myelography was done, found 54 with complications of some form, including shock occurring up to twenty-

four hours after the procedure and hyperesthesia and latent spasms after three hours (*Acta radiol.* 28: 60, 1947. *Abst. in Radiology* 50: 428, 1948). These are thought to be due to irritation of the meninges by the abrodil. This water-soluble substance is rapidly absorbed, but, according to analysis of the spinal fluid after cisternal punctures, not rapidly enough to prevent its appearance at this level one to five hours after injection.

The author reports on 70 cases in which an attempt was made to prevent these complications and to evaluate methods directed to reduce them.

The concentration of abrodil was less in the cisternal fluid if the patient's head was raised instead of lowered (as is usually done after spinal puncture) and even less if the patient assumed an upright position for the first four or five hours. If this procedure is not desirable, it is suggested that 10 to 20 c.c. of spinal fluid be removed by the lumbar route as soon after the examination as possible and replaced by physiologic saline solution in order to reduce the concentration of abrodil reaching the basilar cisterns and cerebral meninges.

Two diagrams.

JOHN S. SCOTT, M.D.  
Indiana University

**The Cervical Disc Syndrome.** E. S. James and P. H. Decter. *Canad. M. A. J.* 61: 456-462, November 1949.

The authors describe the significant contributions to the literature that have advanced our knowledge of herniated cervical intervertebral disks, and present a study of their own reviewing 100 consecutive cases showing radiological signs. They believe that herniated cervical disk is probably as common a cause of brachial neuritis as herniated lumbar disk is of sciatica.

The most common symptom of herniated cervical disk is pain in the shoulder, which frequently radiates down the arm and up into the neck. Neurological changes can sometimes be demonstrated by the examiner, but more often not, especially in the early cases. Probably the most constant physical sign is pain on pressure over the interspace of the affected disk just lateral to the cervical spines. This maneuver is sometimes successful in producing the typical radiation of pain down the arm. A chart is presented with the aid of which the involved disk can be located according to the distribution of the pain radiating down the arm.

The diagnosis is made radiographically by the demonstration of a narrowed intervertebral disk space in a patient who has suggestive clinical symptoms. Myelographic studies can be used for confirmation, but the authors do not urge this unless one is prepared to operate if the findings are positive.

Conditions to be differentiated are: bursitis, tendinitis, osteo-arthritis of the shoulder, angina pectoris, coronary occlusion, and mastitis. The authors believe the scalenus anticus syndrome is probably most often simply a symptom of herniated cervical intervertebral disk.

Conservative treatment is recommended. Operative treatment is reserved for severe and intractable cases. One drawing; 1 table.

T. FREDERICK WEILAND, M.D.  
Jefferson Medical College

**Fusion of Vertebrae Following Non-infectious Disturbance in the Zone of Growth.** Folke Knutsson. *Acta radiol.* 32: 404-406, Dec. 31, 1949.

A non-infectious disturbance in the zone of growth of the vertebral body resembling Scheuermann's disease in

its initial phase is described. Later the cartilage of the anterior portion of the intervertebral space disappears and osseous fusion occurs. In the posterior portion the growth proceeds normally and a progressive curvature results. The condition must be differentiated from congenital malformation and infectious spondylitis. A single case is reported.

Two roentgenograms. DAVID C. GASTINEAU, M.D.  
Indiana University

**Variation in Extension of the Metacarpo-Phalangeal and Interphalangeal Joints of the Thumb.** H. Harris and J. Joseph. *J. Bone & Joint Surg.* 31-B: 547-559, November 1949.

The authors investigated the variation in extension of the interphalangeal and metacarpo-phalangeal joints of the thumbs of 133 male and 100 female Europeans, 31 male Indians, and 30 male Africans. In each subject a lateral view of the thumbs was taken with the metacarpal joint extended fully, with the thumb midway between abduction and adduction and the thumbnail at right angles to the film. Standard longitudinal axes for the three bones were found on the roentgenograms, and the angles between them were measured to the nearest half degree.

Using this method of study the authors found that there is considerable variation between individuals in the maximum extension of both joints of the right and left thumbs in all groups studied, that the distribution for each joint in both thumbs in all groups is fairly symmetrical, and that there is a high correlation between the right and left thumbs for both joints in all groups. The mean angle of extension at the right and left metacarpo-phalangeal joints in all groups is similar, though female Europeans show a significantly greater mean angle of extension than male Europeans. The mean interphalangeal angle of extension of male Europeans is significantly greater than that in female Europeans, and the mean in the Indian and African groups is significantly greater than in the male European group. The authors also found that many subjects in all groups can increase extension at the metacarpo-phalangeal joints after flexing the carpo-metacarpal joints. Marked hyperextension (over 40°) is more frequent in the left than in the right thumb, in females than in males, and in male Indians than in male Europeans and Africans. It was also noted that some cases of extreme hyperextension could not be differentiated from subluxation on the films. The maximum extension at the interphalangeal joints was found not to be related to the presence of a sesamoid bone in the anterior part of the capsule of the joint. The study also showed that the surfaces of the metacarpo-phalangeal joints vary considerably in shape. Those which are flat form about 10 per cent of the sample and do not show hyperextension. The greatest degree of extension was found in those individuals whose first metacarpal bone had a round head.

The authors conclude that the factors influencing the amount of extension at the interphalangeal joint is the degree of laxity of the anterior capsule. The problem at the metacarpo-phalangeal joint is more complex, with both the capsule and the shape of the joint surfaces playing important roles.

Thirty-seven roentgenograms; 20 histograms; 9 tables.

WILLIAM SMITH, M.D.  
Louisville, Ky.

**A Congenital Abnormality of the Trapezium and First Metacarpal Bone.** A. F. Rushforth. *J. Bone & Joint Surg.* 31-B: 543-546, November 1949.

The author presents the case of a 65-year-old white woman who had abnormal hands. On each side there was marked prominence of the base of the first metacarpal. The range of movement at the carpo-metacarpal joint was limited, particularly abduction and extension. Opposition, however, was almost normal.

Roentgenograms showed that the abnormality was almost symmetrical and consisted of enlargement of the base of the metacarpal and gross alteration in the shape of the trapezium, which was longer than normal and presented an acute angle on the radial aspect. Each trapezio-metacarpal joint was deformed. There was a separate ossicle in each hand, on the right at the outer angle of the trapezium forming part of the joint surface, and on the left on the palmar surface, seen more clearly in the lateral view, in the position of the tuberosity. The trapezio-metacarpal joints were obviously arthritic, with narrowed joint spaces, but were also distorted as if they had migrated proximally.

The author reviews the literature and explains this deformity on Pfitzner's plan. (Pfitzner produced a plan of the hand showing the numerous cartilaginous centers which could occur in the embryo and persist as separate bones in the adult.) The condition is quite distinct from osteoarthritis of the trapezio-metacarpal joints.

Seven illustrations.

WILLIAM SMITH, M.D.  
Louisville, Ky.

**Osteoarthritis of the Trapezio-Metacarpal Joint.** Ch. Lasserre, D. Pauzat, and R. Derennes. *J. Bone & Joint Surg.* 31-B: 534-536, November 1949.

The authors point out that the trapezio-metacarpal joint is an important site for osteoarthritis. In order to be diagnostic, films of this area must be made with the hand and forearm fully pronated.

In early trapezio-metacarpal arthritis the following radiographic changes may be observed in the joint: (a) narrowing of joint space, (b) subchondral condensation of bone, (c) lateral subluxation, (d) osteophyte formation on the lateral borders of the trapezium and the metacarpal, (e) deformity of the medial and distal angle of the trapezium.

In gross trapezio-metacarpal arthritis, radiographs show clear details of the lesion. In extreme cases dislocation can be so marked that the base of the metacarpal is opposite the trapezio-scapoid joint. The joint space is not visible but fluoroscopy during movement shows that it is partly preserved. In all cases the greatest deformity and largest osteophytes are at the distal and medial angle of the trapezium.

The recommended treatment is immobilization of the joint in abduction at the first sign of arthritic changes.

Eleven illustrations including 8 roentgenograms.

WILLIAM SMITH, M.D.  
Louisville, Ky.

**Impression Fractures in the Caput Humeri in Connection with Electroshock.** Tore Sylwan. *Acta radiol.* 32: 455-460, Dec. 31, 1949.

In 1948, 5 cases of impression fracture in the caput humeri arising as a complication of electroshock treatment for mental disease were encountered at the South Stockholm Hospital. A total of 150 patients were given electroshock treatment during the year.

The fractures occur medial to the lesser tubercle. On an ordinary anteroposterior roentgenogram of the head of the humerus in inward rotation, the fracture is seen as a thin marginal area separated from the substantia spongiosa by an even rim of increased density. This rim can easily be mistaken for the proximal demarcation line of the lesser tubercle, and this type of fracture is easily overlooked if the possibility of its presence is not borne in mind. If the impression is shallow, views must be taken with the ray at a tangent to the part of the caput humeri under examination.

There is strong reason to believe that the fractures arise as the result of a temporary dorsal dislocation of the shoulder during the spasm caused by the shock, in connection with which the medial portion of the caput humeri is pressed against the posterior edge of the glenoid cavity.

Nine roentgenograms.

F. R. McCREA, M.D.  
Indiana University

**Synovial Osteochondromatosis. Two Uncommon Examples.** J. F. Curr. Brit. M. J. 2: 1020-1022, Nov. 5, 1949.

Two unusual cases of osteochondromatosis are presented, one involving the shoulder joint and the other a bursa posterior to the ankle joint.

In the shoulder there were about 350 loose bodies, some of which showed bone formation in their centers. The synovial membrane was very actively proliferating, and it was felt that a recurrence was inevitable. Adhesions and hemorrhage prevented the surgeon from removing as much of the synovia as he wished. The shoulder is rarely the site of this condition, following, in order of frequency, the knee, elbow, ankle, and hip.

The second case showed a much smaller number of loose bodies in the joint, the unusual feature being the occurrence in a bursa. Recovery followed removal of the osteochondromata and excision of the bursa.

As long as the "loose" bodies are attached by their pedicles to the synovial lining, the blood supply makes possible the formation of bone. Once they actually become loose bodies, bone formation can no longer take place. The cartilage of which they are composed is able to obtain sufficient nourishment from the synovial fluid to proliferate and increase the size of the nodule. Calcification of the periphery may take place later.

Two roentgenograms; 1 photomicrograph; 1 photograph.

ZAC F. ENDRESS, M.D.  
Pontiac, Mich.

## GYNECOLOGY AND OBSTETRICS

**Absorption of Radiopaque Substances Used in Hysterosalpingography. A Comparative Study of Various Aqueous and Oily Media.** Willis E. Brown, Agnes F. Jennings, and J. T. Bradbury. Am. J. Obst. & Gynec. 58: 1041-1053, December 1949.

A study of 118 cases to determine the clinical suitability and absorbability of five radiopaque media used in hysterosalpingography was made. The media used were rayopaque, skiodan, lipiodol, iodochlorol, and lipiodine. A fractional method of injection without manometric control was employed, and a total of 8 to 12 c.c. of the opaque substance was usually injected. In each case, an attempt was made to demonstrate tubal filling and peritoneal spill and to follow absorption from the peritoneal cavity in serial films. In the case of

aqueous media, films were taken at ten-minute intervals; in the case of oily media films were made at monthly intervals.

The individual characteristics of each medium as indicated by this study are reported as follows:

1. *Rayopaque*: Very rapid absorption, excretion by the kidneys. Radiographically satisfactory.
2. *Skiodan*: Very rapid absorption, renal excretion. Too rapid emptying of the tubes. Radiographically satisfactory, but tubal details not clearly shown.
3. *Lipiodol*: Very slowly absorbed, persisting as long as fourteen months. In 2 patients "oil-retention" cysts developed. Excellent tubal visualization. Radiographically excellent.
4. *Iodochlorol*: Slowly absorbed. Excellent tubal visualization. Radiographically excellent.
5. *Lipiodine*: Slowly absorbed, but most rapidly absorbed of the oily agents used. Too low viscosity, resulting in poor tube detail because of too rapid peritoneal spill. Radiographically excellent.

The evidences of untoward reactions encountered were as follows:

1. *Rayopaque*: Leukocytosis, slight fever, and lower abdominal pain in one patient with evidence of tubal disease. Her symptoms responded promptly to antibiotics. In one patient who had a history of allergy, urticaria developed.
2. *Skiodan*: Generalized urticaria in 3 patients having no history of allergy.
3. *Lipiodol*: Fever, leukocytosis, and lower abdominal pain four days after injection in one patient; two cases of "oil-retention" cysts.
4. *Iodochlorol*: No untoward clinical reactions.
5. *Lipiodine*: Two cases of severe septic reaction.

The authors conclude that the aqueous radiopaque agents are preferable for hysterosalpingography because of their rapid absorption and relative freedom from the many untoward reactions encountered with the oily media.

Twenty-eight roentgenograms; 2 photomicrographs; 3 tables.

HARVEY J. THOMPSON, JR., M.D.  
Jefferson Medical College

**Experience with Hysterosalpingography (Exclusive of Determination of Tubal Patency in Sterility).** O. Käser and H. Deuel. Radiol. clin. 18: 349-360, November 1949. (In German)

The authors emphasize that hysterosalpingography is of great diagnostic value to the gynecologist, as evidenced by the varied applications made of it during the last two years at the Women's Hospital at Basel.

It has proved helpful in the diagnosis of extra-uterine pregnancies, where a water-soluble contrast medium was used with great precaution in order to prevent a reflux into the blood and lymph vessels. Five diagnostic points are described: hypotonus of the uterus, filling defects of the uterine cavity, obstruction of the tubes, dilatation of the lumen or irregular depot formation in the region of the imbedded ovum, and changes in patent tubes. Seven out of 9 cases showed tubal pregnancies; one was an intra-uterine abortion, and one was diagnosed as a probable functional bleeding of the uterus.

Intrauterine pregnancy is a contraindication for hysterosalpingography. It was used, however, erroneously in 3 cases, in which myomas and polyps were discovered.

Ten cases, of which short histories are given, deal with the diagnosis of myomas of the uterus and of hyper-

plasia of the endometrium with polyposis. The roentgenogram revealed a hypertonus of uterus and deformation of the uterine cavity.

Sixteen out of a total number of 181 cases of unsuccessful castration by roentgen rays are discussed. In none of these cases was the failure attributable to insufficient x-ray dosage. Five cases with submucous myomas are cited, and one case with a large polyp.

The value of hysterosalpingography in malformations of the uterus, including infantilism and hypoplasia, in carcinoma of the corpus, and in the diagnosis of tuberculosis of the tubes is briefly discussed.

In 18 out of 520 cases, a reflux of the iodized oil was observed without serious complications. Finally, it is emphasized that even under very slight pressure this reflux into the blood and lymph vessels can occur, and that manometer readings are not an adequate safeguard.

Seven illustrations.

EUGENE F. LUTTERBECK, M.D.  
Cook County Hospital, Chicago

**Diverticula of the Female Urethra. Report of Twenty Cases.** R. Theodore Bergman. *Urol. & Cutan. Rev.* 53: 590-593, October 1949.

The author presents a study of 20 cases of urethral diverticulum in the female. The fact that a number of these cases had been previously seen and treated without recognition of the condition indicates that the female urethra is often not given the careful study it deserves. The youngest patient was thirty years of age and the oldest sixty-four.

A palpable mass, pyuria, and pain were the symptoms most frequently encountered. Less frequent manifestations in this series were frequency, burning, hematuria, and discharge.

The diagnosis of urethral diverticulum can usually be made by palpation, urethroscopy, and urethrography. Cystoscopy with the right-angle or retrograde lens does not adequately visualize the diverticular orifice in the urethra. Palpation of the urethra over the cystoscope often provides valuable information as to the presence of a sac, its size, and whether or not it empties. It also helps in determining the presence or absence of calculi.

Roentgen visualization is not essential for a diagnosis of diverticulum of the urethra, but urethrography is a distinct aid, particularly in ascertaining the presence, number, size, and capacity of the diverticular sacs. For this purpose the Keyes-Ultzmann metal cannula as modified by Rubin for uterotubal insufflation is a convenient instrument. The medium used is a mixture of equal parts of an aqueous lubricating jelly and skiodan. The anteroposterior film alone is usually diagnostic for routine work. Oblique radiographs are of value, however, where multiple sacs are present.

Urethral diverticulum must be differentiated from cysts of the vaginal wall and infections of Skene's gland. The treatment is surgical removal of the diverticulum through the vaginal wall.

Seven roentgenograms.

HUGH A. O'NEILL, M.D.  
Cleveland, Ohio

**Female Bladder and Urethra Before and After Correction for Stress Incontinence.** Andrew A. Marchetti. *Am. J. Obst. & Gynec.* 58: 1145-1153, December 1949.

Marchetti reports the results of suprapubic vesico-urethral suspension, as described by V. F. Marshall

*et al.* (*Surg., Gynec. & Obst.* 88: 509, 1949), in 12 patients with urinary stress incontinence. Cystography played an important part of the preoperative and postoperative evaluation. Three films of the bladder filled with opaque material were taken in each case, before and after operation: (1) recumbent, (2) erect, and (3) erect while voiding. Failure of the pelvic floor, especially of the levator ani, to support the vesical sphincter mechanism was frequently associated with loss of urinary control. Postoperative cystography revealed the considerable degree of elevation of the bladder and its outlet effected by the operation. It also demonstrated that the procedure fixes the urethra to the posterior surface of the symphysis pubis without distortion.

In the discussion following the presentation of Dr. Marchetti's paper at the 72nd Annual Meeting of the American Gynecological Society, Dr. R. Gordon Douglas pointed out the value of a lateral cystogram in the demonstration of the position of the bladder neck.

Nineteen roentgenograms.

T. F. WEILAND, M.D.  
Jefferson Medical College

**Displacement of the Bladder and Urethra During Labour.** P. Malpas, T. N. A. Jeffcoate, and Ursula M. Lister. *J. Obst. & Gynaec. Brit. Emp.* 56: 949-960, December 1949.

The movement of the bladder and urethra in labor was studied by cystograms. The authors summarize their findings, on the basis of lateral views, as follows: "(a) At the onset of labor the bladder base and the urethrovesical junction are at the level of a line joining the lower border of the symphysis pubis and the tip of the sacrum. (b) Dilatation of the cervix and thinning of the lower uterine segment does not directly influence the position of the bladder base. (c) As the presenting part descends, the bladder base is rolled up from behind forwards until it comes in line with the urethra. Both bladder base and vesico-urethral junction then move towards the symphysis. (d) In the normal case there is not much upward movement of the bladder neck, nor is there significant lengthening of the urethra. Part of the bladder just above the bladder neck, which becomes funnel-shaped as viewed from the side, usually remains behind the symphysis. (e) The extent of the displacement of the bladder and urethra depends largely on the relative sizes of the presenting part and the pelvic cavity. When the cavity is cramped and there is mid-pelvic arrest of the head, the bladder neck may lift to the level of the top of the pubis and the urethra is somewhat lengthened. Such a state of affairs may indicate the need for Caesarean section."

In cases of stress incontinence it is suggested that the essential lesion is a failure of the fascia investing the bladder base behind the urethro-vesical junction to recover tone.

Seven roentgenograms; 35 drawings.

MORTIMER R. CAMIEL, M.D.  
Brooklyn, N. Y.

**Value of Upright Roentgenograms of the Maternal Pelvis at or Near Term with Particular Reference to Placenta Praevia.** H. R. Crews, A. O. Hampton, and J. P. Moore. *Am. J. Roentgenol.* 62: 707-714, November 1949.

The authors state that their purpose in presenting this paper is to emphasize the value of upright roentgeno-

grams of the maternal pelvis. For the past three years all pregnant patients at Garfield Memorial Hospital, Washington, D. C., have had lateral and postero-anterior roentgenograms made with the patient horizontal, and lateral and anteroposterior roentgenograms made with the patient upright. In the first procedure, the central ray is directed at the center of the pregnant uterus, while in the latter it is directed through the pelvis 1 inch above the level of the greater trochanter of the femur.

The following observations were made: 1. If the placenta is definitely visualized in the fundus uteri and if the head enters or centers upon the pelvic inlet, there is no evidence of placenta praevia or disproportion; 2. If the placenta is visualized in the mid or lower portion of the uterus and the head is displaced in relation to the inlet, with the patient upright, the placenta is marginal; 3. Non-visualization of the placenta and upward displacement of the head without cephalopelvic disproportion indicates a centrally located placenta; 4. Measurement of the size of the head and the pelvic inlet will make disproportion apparent; 5. Visualization of the placenta in the fundus uteri and displacement of the head without disproportion are indicative of a pelvic tumor.

A distended bladder or unruptured membranes protruding through the cervix may simulate a centrally located placenta praevia or pelvic tumor.

The authors feel that this simple examination eliminates elaborate fetal head and pelvic measurements.

Eight sketches and twelve photographs accompany the article.

J. B. SCRUGGS, M.D.  
University of Arkansas

### THE GENITO-URINARY SYSTEM

**Renal and Ureteral Fistula of the Visceral and Cutaneous Types: A Report of Four Cases.** Benjamin S. Abeshouse. *Urol. & Cutan. Rev.* 53: 641-674, November 1949.

A comprehensive review of renal and ureteral fistulae is presented, covering the literature thoroughly and including a bibliography of 306 references, appropriately classified.

The collected cases of spontaneous renal and ureteral fistula, numbering 339, including 4 cases reported by the author, are tabulated as follows:

#### A. Reno-visceral, 226 cases

1. Reno-gastric.....	5
2. Reno-duodenal.....	9
3. Reno-colic.....	89
4. Reno-peritoneal.....	52
5. Reno-pulmonary.....	59
6. Reno-vesical.....	4
7. Reno-vaginal.....	3
8. Reno-ureteral.....	3
9. Reno-renal.....	2

#### B. Renal-cutaneous, 51 cases

1. Reno-lumbar.....	32
2. Reno-inguinal.....	16
3. Reno-umbilical.....	1
4. Reno-gluteal.....	1
5. Reno-crural.....	1
6. Reno-penile, scrotal or perineal (uncomplicated).....	0

#### C. Uretero-visceral, 52 cases

1. Uretero-gastric.....	0
2. Uretero-duodenal.....	1
3. Uretero-jejunal.....	1
4. Uretero-colic.....	10
5. Uretero-peritoneal.....	7
6. Uretero-pulmonary.....	0
7. Uretero-vesical.....	6
8. Uretero-vaginal.....	10
9. Uretero-ureteral.....	16
10. Uretero-arterial.....	1

#### D. Uretero-cutaneous, 10 cases

1. Uretero-lumbar.....	5
2. Uretero-inguinal.....	4
3. Uretero-gluteal.....	1
4. Uretero-penile, femoral, perineal (uncomplicated).....	0

The etiology of renal and ureteral fistula is also summarized in table form, as follows:

#### I. Spontaneous

##### A. Renal origin

1. Infections—*i.e.*, tuberculosis, pyelonephritis, cortical abscess
2. Lithiasis—*i.e.*, stone in calyx, pelvis or ureter
3. Obstructive lesions—*i.e.*, hydronephrosis, pyonephrosis
4. Renal neoplasms—*i.e.*, rupture, perirenal hematoma
5. Miscellaneous
  - (a) Renal echinococcus disease
  - (b) Renal actinomycosis
  - (c) Renal infestation: *Ascaris lumbricoides*, *Strongyloides intestinalis*
  - (d) Syphilis—*i.e.*, gumma.
  - (e) Periarthritis nodosa—*i.e.*, perirenal hematoma

##### B. Perirenal origin

1. Suppurative perinephritis or perinephric abscess

##### C. Juxta-renal disease

1. Tuberculous osteomyelitis of vertebra or ribs
2. Pyogenic osteomyelitis of vertebra or ribs
3. Extension of abscess from adjacent areas—*i.e.*, subphrenic, subdiaphragmatic, dural, iliac nodes
4. Retroperitoneal abscess of intestinal origin—*i.e.*, appendiceal, duodenal, biliary, pancreatic, intestinal
5. Extension of abscess from lower urinary tract and genitals in male—*i.e.*, prostate, seminal vesicles, urethra, bladder
6. Extension of abscess from genital tract in female—*i.e.*, salpingitis, oophoritis, endometritis

#### II. Traumatic

1. Direct injuries to kidney, pelvis, or ureter—*i.e.*, crushing, etc.
2. Penetrating injuries to kidney, pelvis or ureter—*i.e.*, gunshot, shrapnel, stabbing, etc.
3. Indirect injuries to kidney, pelvis or ureter—*i.e.*, violent muscular effort

III. Postoperative

1. Following operations on kidney or ureter
  2. Following gynecological or obstetrical operations
  3. Following operations on lower intestinal tract
- The most common etiologic factor is advanced destructive renal disease, as lithiasis, pyonephrosis, hydronephrosis, tuberculosis, and perirenal suppuration. Formerly the correct diagnosis was usually made at operation or autopsy. At present the most important diagnostic measure is cystoscopy with retrograde pyelography. Other valuable roentgenologic measures for delineating the fistulous communications are the injection of iodized oils in cutaneous and pulmonary fistulae and barium studies in cases of colic fistula. Excretion urography is of little value.

Ten roentgenograms; 5 drawings.  
S. F. THOMAS, M.D.  
Palo Alto, Calif.

Intravenous Urography in the Study of Vesical Neck Obstructions. William J. Engel. Am. J. Roentgenol. 62:661-669, November 1949.

The author reviews the indications for intravenous urography in the study of vesical neck obstructions and presents his modifications of the procedure. Films are taken at five, fifteen, thirty, and sixty minutes after injection of intravenous diodrast. At the thirty-minute interval, an additional 10 X 12-inch film is made to include the lower ureters, bladder, prostate, and urethra. According to the author this affords a more detailed cystogram. Following the last film, if desired, a residual urine film may be obtained after the patient has voided, thereby making it possible to ascertain the amount of urine remaining in the bladder. The author points out that his routine affords a fractional function test, which constitutes an additional refinement of the usual intravenous pyelographic technic.

Findley and his co-workers (J. Urol. 48: 119, 1942) found that the normal kidneys excrete 40 to 50 per cent of the diodrast in the first thirty minutes following injection, and that reductions in the rate of iodine excretion are roughly proportional to the variations in the urea clearance. Kornblum and Fetter (Am. J. Roentgenol. 48: 770, 1942) found the intravenous pyelographic technic to be 70 per cent in agreement with the fractional phenolsulfonphthalein test, and Braasch and Emmett (J. Urol. 35: 630, 1936) found 78 per cent agreement with the indigo carmine test.

Vesical neck obstructions are of four types: (1) contractures and fibrotic median bars; (2) intravesical enlargement; (3) subvesical or intra-urethral enlargement; (4) carcinomas. Types 2 and 3 may exist in combination. Hypertrophy of the trigone may be recognized by a transverse crescentic shadow whose concavity is toward the dome of the bladder.

In the urograms, subvesical enlargement becomes manifest by an extrinsic mass impression and angulation of the lower ureters of a varying degree, causing, in extreme cases, a reverse curve or "fish-hooking." Ureteral angulation should be regarded with some concern. The author has observed several patients who, upon first examination, presented a picture of moderate prostatic intrusion with early angulation of the lower ureters, but with normal ureters and renal pelvis. Examination of the same patients who returned after several years without treatment showed extensive bilateral hydro-ureter and hydronephrosis with impaired renal function.

Ureteral angulation, therefore, should be regarded as an indication for the operative correction of prostatic obstruction.  
Eleven radiographs; 3 drawings.  
E. S. KEREKES, M.D.  
University of Arkansas

Bilateral Megalo-Ureter in a Child. Return to Normal with Prolonged Control of Infection. Walter Heymann and James F. Martin. J. Pediat. 35: 618-624, November 1949.

A case is reported of a 20-month-old female with bilateral, possibly congenital, megaloureters with hydronephrosis. Cystoscopic examination failed to reveal any evidence of a bladder neck obstruction. After streptomycin had sterilized the urine and infection had been controlled uninterruptedly by continuous sulfadiazine medication for many months, the patient showed improvement in appetite, nutrition, and weight. After the urine had been normal for one year, the sedimentation rate was 9 mm. and radiographic evidence of improvement was obtained. Cystograms and intravenous pyelograms were normal following thirty-two months of chemoprophylaxis.

Ten roentgenograms.  
HOWARD L. STEINBACH, M.D.  
University of California

TECHNIC; CONTRAST MEDIA

Is a Roentgenogram of Fine Structures a Summation Image or a Real Picture? J. E. J. Resink. Acta radiol. 32: 391-403, Dec. 31, 1949.

The object of the study reported here was to determine whether a roentgenogram of small details or fine structures is an actual image or the result of superposition of the shadows of many foci situated one behind the other (summation theory). Experiments were done with both non-anatomical phantoms and anatomical preparations, with some of these objects being just supraliminary or just infraliminary. Producing objects with these latter characteristics was done by leaving a test object on the film for a fraction of the exposure only. Then the fraction was gradually reduced until the object produced no distinguishable contrast.

Some of the findings were as follows: (1) No image is obtained when a roentgenogram is made of an accumulation of many infraliminary elements of an object unless these latter are equally large and almost entirely cover each other.

(2) An accumulation of objects that are just visible gives an image that grows less clear as the number of layers of such objects increases.

(3) When the roentgenogram shows an accumulation of many elements that are strongly supraliminary and the images are equal in respect to contrast, the picture is dominated by superposition images.

(4) A roentgenogram of elements of different contrasts reveals that the most supraliminary elements dominate the photograph while the others give a vague or unanalyzable background.

(5) To give rise to an image, the radiation contrast must be greater when there is a background.

(6) Stereoscopy and the other experiments seem to indicate that the roentgenograms reproduce actual details and not summation images.

Six illustrations.  
RICHARD C. DATZMAN, M.D.  
Indiana University

**Subclavian Angiography by Arterial Catheterization. Visualization of Metastatic Tumor in the Upper Thoracic Aperture.** Stig Radner. *Acta radiol.* 32: 359-364, Dec. 31, 1949.

Following a brief review of the literature on venous and arterial angiography, the author describes his technique for subclavian arterial angiography. This method is presented as a means of demonstrating abnormal circulation in branches arising from the medial portion of the subclavian artery supplying the parathyroid glands, the thymus, and parts of the thyroid gland.

The method includes premedication with 8 to 10 c.c. of a 2.5 per cent solution of papaverin hydrochloride and morphine sulfate to reduce arterial spasm and pain incident to the injection of the contrast medium. The radial artery is catheterized and a ureteral catheter is inserted under fluoroscopic visualization to the subclavian artery. A sphygmomanometer cuff is placed around the arm and inflated above the systolic blood pressure just before injection. In adults, 15 c.c. of a 35 per cent solution of diodrast is injected rapidly. One exposure is made immediately after injection and one three or four seconds later.

One case is reported in which a hypernephroma had been removed twelve years previously. Roentgen examination showed a destructive lesion in the lumbar region thought to be osteitis fibrosa or a metastasis. Blood calcium was 17 mg. per cent and a surgical exploration of the parathyroids revealed no tumor. Other destructive lesions appeared in the spine, and subclavian angiography was done in an attempt to visualize abnormal circulation of the parathyroid. A walnut-sized collection of vessels was demonstrated on the right side. This tumor was removed. Signs of intracranial complications developed postoperatively and the patient died two days after operation. Postmortem, the features of the tumor removed and the metastatic areas in the spine were found histologically to be those of hypernephroma.

Three roentgenograms. JOHN S. SCOTT, M.D.  
Indiana University

**Plebography in Chronic Venous Insufficiency of the Lower Extremity. A Preliminary Report.** I. C. Højensgård. *Acta radiol.* 32: 375-390, Dec. 31, 1949.

The author discusses the pathological anatomy and physiology of chronic venous insufficiency on the basis of his recent investigations by direct plebography. The term "chronic venous insufficiency" is defined as that chronic condition in which the venous return is impaired because of the destruction of the venous muscular pump mechanism. The most common causes are (1) primary or idiopathic varicosities (insufficiency of the superficial venous system) and (2) post-thrombotic conditions (insufficiency of the deep venous system).

The studies reported here were made by injection of 20 c.c. of 35 to 50 per cent soluble iodine solution in less than one minute into a vein on the dorsomedial aspect of the base of the great toe, while the patient maintained a vertical position by sitting on a high stool. Serial anteroposterior and lateral radiographs of the leg and lower thigh are made by the use of two x-ray tubes positioned at 90 degrees to each other. The film size is 15 X 40 cm. Two exposures are made in each view because of the variation in the rate of blood flow, which is most rapid in normal and slowest in post-thrombotic subjects. Fifteen seconds should elapse from the com-

pletion of injection until the first exposure is made and then the other exposures are made at ten- to twenty-second intervals. The last exposure takes place at least one minute, preferably two, after injection.

The author stresses the need for the vertical position of the patient in order to show the various valve stations. He disagrees with Bauer with regard to interpretation of the findings of retrograde femoral and popliteal venography and with regard to the selection of the vein to be used for introducing the contrast medium into the venous circulation. A tourniquet is usually applied below the knee at the malleolar level in order to prevent the dye from selecting the superficial pathways.

On the basis of two hundred phlebographic studies of the lower limb, the appearance of the deep veins in normal subjects, in patients with primary varicosities, and in patients with post-thrombotic conditions is described and illustrated.

Twenty-four phlebograms; 1 photograph.

J. A. CAMPBELL, M.D.  
Indiana University

**Electrokymography. Progress of Medical Science.** Russell H. Morgan. *Am. J. M. Sc.* 218: 587-597, November 1949.

Morgan reviews the literature and discusses the rapid evolution of the electrokymograph and its significance. He concludes that with several other recent developments the electrokymograph is raising the curtain on a new era of investigation, an era of physiologic rather than anatomic study. It will be interesting to pursue the many new applications of electrokymography that doubtless will occur in the years to come. The method has certainly shown remarkable potentialities in the first few years since its inception.

**Reaction of the Lung on Bronchography with Viscous Umbradil (Umbradil-Viskös B) (Astra), Umbradil (Astra), and Carboxymethyl Cellulose. An Experimental Investigation on Animals.** B. Hellström and H. Holmgren. *Acta radiol.* 32: 471-485, Dec. 31, 1949.

Umbradil-Viskös B, umbradil, and carboxymethyl cellulose were injected into the bronchial tree in three groups of animals, respectively. Histologically, the changes produced were non-specific and were duplicated by the injection of normal saline. Umbradil seemed to be absorbed directly, while carboxymethyl is ingested by alveolar phagocytes.

Eight photomicrographs. J. G. LORMAN, M.D.  
Indiana University

**Effect of Retained Bronchial Lipiodol on Blood Iodine.** LeRoy Hyde and Bernard Hyde. *J. Lab. & Clin. Med.* 34: 1516-1519, November 1949.

Forty-one determinations of protein-bound blood iodine were done in 30 patients at successive intervals after lipiodol bronchography. All showed an initial marked elevation beyond the normal of 5 to 7 micrograms per 100 ml., with a gradual return to normal, in most instances, after eighteen months. Because of this, blood iodine determinations, as in suspected hyperthyroidism, cannot be used for diagnostic purposes for two years after lipiodol bronchography, and in some cases for as long as four years.

Three charts. CORNELIUS COLANGELO, M.D.  
Chicago, Ill.

**Failure of Antihistaminic Drugs to Inhibit Diodrast Reactions.** Seymour B. Crepea, James C. Allanson, and Lorry DeLambre. *New York State J. Med.* **49:** 2556-2558, Nov. 1, 1949.

The authors state that since certain of the reactions to diodrast could conceivably be of an allergic type, measures used in alleviating known allergic manifestations might be of value in obviating these side-effects.

Recently, a group of drugs called the antihistaminics have been utilized for symptomatic relief of allergic manifestations which are presumed to depend in part on histamine release, and, in addition, they often convey sedative and atropine-like effects. Because of these pharmacologic actions, it was felt that they might be of value in obviating the various untoward reactions to diodrast. With this in view the following studies were carried out.

Three groups of patients, totaling 310, received diodrast in the course of intravenous pyelography. Two of the three groups were given premedication with a known potent antihistaminic drug pyribenzamine or trimeton. Premedication with 100 mg. of pyribenzamine or 50 mg. of trimeton by mouth one hour before the administration of diodrast did not seem to influence the incidence, severity, or type of reactions to diodrast.

Patients having multiple injections of diodrast, particularly that group having previous ill effects, were most apt to have reactions. Patients with a personal history of allergy, especially asthma, were also more apt

to have reactions than those without such a history. Skin or mucous membrane tests do not appear reliable. Patients with a positive test may tolerate the drug without ill effect. Those with negative skin tests may have fatal reactions.

Two tables.

DANIEL WILNER, M.D.  
Atlantic City, N. J.

**Training of the Blind for Dark Room Technicians.** Sherwood Moore. *Am. J. Roentgenol.* **62:** 726-728, November 1949.

The author describes the training process for blind darkroom technicians at the Mallinckrodt Institute of Radiology, St. Louis. Trainees are instructed by the senior technician. The training period includes about two weeks in a pilot darkroom, where they are drilled in loading and unloading films from cassettes and loading and unloading hangers and hangettes until time studies determine their efficiency. After this they are transferred to the actual darkroom.

The author has found the employment of the blind as darkroom technicians most satisfactory, and the technical roentgenographic quality has been of a high order.

[The use of blinded veterans as darkroom technicians was begun at the Philadelphia Naval Hospital in 1944 and was the subject of an earlier Editorial in *Radiology* (Godfrey: *Radiology* **47:** 619, 1946)].

One drawing.

**RADIOTHERAPY**

**Carcinoma of the Eyelid. Analysis of 301 Cases and Review of the Literature.** Charles G. Stetson and Milford D. Schulz. *New England J. Med.* **241:** 725-732, Nov. 10, 1949.

This is a review of 301 primary carcinomas of the eyelid treated in the years 1933 to 1944 inclusive, constituting 2.5 per cent of some 12,000 cancers of the skin observed in this period. The average duration was three and a half years. Sixty per cent of the lesions occurred in males. The lower lid was most frequently involved, and the inner canthus was the second most common site. Eighty-two per cent of the biopsies showed basal-cell carcinoma, and 14.5 per cent were squamous-cell tumors.

Seventy-six per cent of the group were treated by irradiation and 24 per cent by surgery. Apparent cure was ultimately obtained in 97.5 per cent of the group, with 13 per cent requiring a repetition of the original treatment; 2.5 per cent of the cases remained uncontrolled.

Both irradiation and surgical procedures gave adequate results and no statistical difference could be demonstrated between the two methods. Some lesions seem best treated by irradiation, others by surgery, and still others by surgery followed by irradiation. Radium was used in some patients, but less frequently in recent years. Surgery may be used as a sole or primary treatment, or it may be used following irradiation as in plastic repair.

In the irradiation of small lesions, 100-kv. x-rays, unfiltered, are used, at 20 cm. distance; the usual dose is 2,700 to 3,000 r in air. This may be given in a single treatment. If fractionation is desired, daily doses of 1,200 to 1,500 r in air are given to a total of 3,600 to 4,500 r. With more extensive lesions, the daily dose is

500 r in air, to a total of 5,000 to 6,000 r (in air). When the lesion is infiltrating and fixed, especially at the inner canthus, 140 or 200 kv. with 0.25 mm. Cu plus 1 mm. Al are used, with fractionation.

The complications following treatment are scars and defects, inversion of the lid, and stenosis of the tear duct. No radiation cataract has resulted in this series, but particular care is taken to protect the globe. However, if the conjunctiva of the globe is involved, irradiation of the globe will usually produce a cataract. It is a matter of choice between two evils.

Seven photographs; 4 tables.

J. B. McANENY, M.D.  
Johnstown, Penna.

**Results of Surgical and Radiological Treatment in Primary Carcinoma of the Breast. Being a Statistical Analysis of the Complete Experience of Six Public Hospitals in Melbourne During 1940-1941 (Inclusive).** Robert Fowler and Cynthia McCall. *Australian & New Zealand J. Surg.* **19:** 142-149, November 1949.

A statistical analysis was made of 395 cases of breast cancer seen during 1940-1941 (inclusive) in an attempt to determine the method of treatment giving the best percentage of five-year survivals.

Surgery alone in "early" cases [presumably Stage I and II, although this is not entirely clear in the paper] yielded 48.9 per cent five-year survival, while surgery plus radiotherapy [no details of radiotherapy given] yielded 54.6 per cent. The Chi-square test of significance applied to these results showed that the difference was not significant.

Nine tables.

ZAC F. ENDRESS, M.D.  
Pontiac, Mich.

**Lymphatic Spread of Carcinoma of the Cervix and of the Body of the Uterus. A Study of 420 Necropsies.** Erle Henriksen. *Am. J. Obst. & Gynec.* **58**: 924-940, November 1949.

The author's series consists of 420 cases, comprising 64 cases of adenocarcinoma of the corpus uteri and 356 cases of carcinoma of the cervix. The extent of the cervical carcinomas was evaluated according to the League of Nations classification. The series was further divided into treated and non-treated groups, treatment consisting in irradiation, usually with both radium and x-rays.

Twenty-six non-treated and 15 treated cases of cervical carcinoma were studied by careful dissection and multiple sections of the lymph nodes. The results showed involvement of the parametrium in 77 per cent of the non-treated cases, and 33 per cent of the treated cases. Distant metastases occurred in 27 per cent of the non-treated and 53 per cent of the treated cases. In the entire series of 356 cases, however, the incidence of distant metastases was 37.8 per cent of the treated and 32.5 percent of the non-treated, an insignificant difference.

The routes of lymphatic spread followed a constant course from the site of the primary lesion to the parametrium, primary group nodes, secondary group nodes, and finally extension beyond the pelvis. In the entire series of cervical carcinomas, the probable arresting effect of irradiation was emphasized by the difference in node group involvement.

The routes of lymphatic spread of endometrial carcinoma are less constant, there being involvement of the same node groups as in cervical carcinoma, or by-passing of the primary groups with the direct metastases to the inguinal or the aortic nodes. The numerous intercommunicating lymphatic vessels account for the unpredictable sites of metastases.

Uremia was the most frequent cause of death in both cervical and endometrial carcinoma.

Histopathological evidence did not prove that metastatic nodes may be sterilized by irradiation, though necropsy findings suggested the possibility of such effect.

[This same series of cases is analyzed in the author's discussion of Dispersion of Cancer of the Cervix in the Symposium on Cervical Carcinoma, published in *Radiology* **54**: 812, June 1950.—Ed.]

HARVEY J. THOMPSON, JR., M.D.  
Jefferson Medical College

**Results of an Experimental Therapy of Carcinoma of the Cervix.** J. L. McKelvey, K. W. Stenstrom, and J. S. Gillam. *Am. J. Obst. & Gynec.* **58**: 896-904, November 1949.

The authors present an analysis of results of treatment in 297 cases of carcinoma of the cervix at the University of Minnesota Hospitals from 1939 to Jan. 1, 1949. The diagnosis was confirmed by biopsy in every case. The League of Nations Cancer Committee rules were applied and their staging used.

It was arbitrarily decided to deliver 3,000 tissue roentgens by x-ray diffusely to the whole pelvis, including the tumor, over as close to twenty-eight days as possible. The technic varied only slightly over the period under consideration. Up to June 1942, the factors were 220 kv., 1.0 mm. Cu plus 1.0 mm. Al filtration, h.v.l. 1.7 mm. Cu, target-skin distance 60 and 70 cm.; after June 1942, 400 kv., 0.44 mm. Sn plus 0.25 mm. Cu

plus 1.0 mm. Al filtration, h.v.l. 3.9 mm. Cu, target-skin distance 70 and 80 cm. As a rule, five fields have been used: one anterior, one posterior right oblique, one posterior left oblique, one right lateral, and one left lateral. One field was treated each day, receiving 300 to 350 r/air. On the last day of x-ray treatment, radium was inserted to be left in place for 100 hours. Under ideal anatomical conditions, two intra-uterine sources in tandem and three vaginal sources in the Kaplan colpostat were used. Each contained 10 mg. of radium, giving a total dose of 5,000 mg. hr.

The absolute five-year cure rates with the standard deviations were as follows: for all stages, 53.6 per cent (s.d.  $\pm$  2.8 per cent); Stage I, 80.2 per cent (s.d.  $\pm$  4.0 per cent); Stage II, 54.1 per cent (s.d.  $\pm$  4.8 per cent); Stage III, 29.5 per cent (s.d.  $\pm$  5.2 per cent); Stage IV, 1 of 16 patients.

There can be no doubt that accurately applied irradiation offers the most effective tool in the attack on carcinoma of the cervix and that the surgical approach should be restricted to special circumstances. Some method must be found, however, which will allow recognition, at least by the time therapy is complete, of those tumors which will fail to respond to irradiation. Histologic studies on material taken on the day x-ray was completed and radium applied were of questionable value in this study.

Five tables.

ROBERT H. LEAMING, M.D.  
Jefferson Medical College

**Further Studies on the Effect of Irradiation Therapy for Carcinoma of the Cervix upon the Urinary Tract.** Houston S. Everett, C. Bernard Brack, and George J. Farber. *Am. J. Obst. & Gynec.* **58**: 908-919, November 1949.

In 1939, one of the authors reported on a series of 46 patients who were treated by irradiation for carcinoma of the cervix (*Am. J. Obst. & Gynec.* **38**: 889, 1939). Thirty-three of these patients were studied urologically before and at intervals after completion of therapy. Thirteen cases in this group, in which the cancer was known to be cured, were restudied. Four had vesicovaginal fistula (2 with rectovaginal fistula); 3 complete occlusion of one ureter with functionless kidney (2 of these in patients with vesicovaginal fistula); 6 urethral stricture with hydro-ureteronephrosis (slight or moderate in 4 cases); 4 had no urological lesions.

In this earlier series, many of the patients who developed severe urinary tract damage received no x-ray therapy, and several of them had received less than 3,000 mg. hr. of radon. However, in all the radon had been administered without anesthesia and in most instances with less careful packing of the vagina than is possible in the anesthetized patient.

For purposes of comparison, a series of cases treated in 1940-1942, and thus permitting five-year observations, is presented. Treatment in these cases was by a combination of radium and roentgen rays. Prior to 1941, roentgen therapy was given at 200 kv.p., with a dose of 2,000 r to each of two anterior and posterior 15 X 15-cm. portals, at a skin-target distance of 50 cm. The half-value layer was 1.9 mm. of copper. After 1941 most of the patients were treated at 400 kv.p., with 250 r to each of two fields three times a week until 10,000 r, measured with back-scatter, was administered, 2,500 r to each of four fields. The skin-target distance was increased to 70 cm. The half-value layer was 5 mm. of copper. The radium dosage was 4,800 mg. hr., in two

twenty-four hour applications of 100 mg. of radium, with an interval of two weeks between treatments. In this series there was no urinary tract damage in the patients who survived five years or more.

In a third small series of patients the same x-ray dosage was used, but the radium dosage was increased to 6,000 mg. hr. by increasing the amount of radium by 25 percent but leaving the time required for administration the same. In this instance there was a high percentage (31 per cent) of severe post-irradiation reactions.

The authors demonstrate that the urological study of patients before and at repeated intervals subsequent to treatment of carcinoma of the cervix by irradiation therapy is a valuable procedure. Radium is potentially more dangerous than x-ray therapy in so far as the production of urinary tract damage is concerned. The potential danger to the urinary tract and other normal structures from radium irradiation is reduced by achieving the desired milligram-hour dosage with smaller amounts of radium administered over larger periods of time.

Eleven illustrations, including 8 roentgenograms.

ROBERT H. LEAMING, M.D.  
Jefferson Medical College

**Ovarian Carcinoma. A Review of 200 Primary and 51 Secondary Cases.** Equinn W. Munnell and Howard C. Taylor, Jr. *Am. J. Obst. & Gynec.* **58:** 943-955, November 1949.

The authors review the end-results in 200 cases of primary carcinoma of the ovary seen at the Sloane Hospital for Women (New York) from 1922 to 1943. The over-all relative five-year survival rate for these cases was 30.8 per cent, and the absolute survival rate was 27.5 per cent.

Papillary serous cystadenocarcinomas made up almost two-thirds of the total series. Papillary pseudomucinous cystadenocarcinoma and granulosa-cell tumors were the two most favorable types, the relative cure rate for each being above 60 per cent.

The extensive loss of life (almost 60 per cent) within the first year and a half after treatment is begun testifies to the malignancy of ovarian cancer. The best five-year survival rates are obtained when there has been no spread beyond the ovaries; whether ovarian involvement is unilateral or bilateral does not seem important in prognosis, but as soon as spread outside the ovaries occurs, the chances for five-year survival drop precipitously.

Surgery remains the fundamental part of the treatment of carcinoma of the ovary. The authors agree with Meigs that radical surgery should be performed if the tumor is papillary, with the possible exception of rare instances in which the patient is young and childless. Here, if the gross appearance of the tumor suggests low-grade malignancy and if the opposite ovary seems perfectly normal, the latter and the uterus may be retained. As a general rule, however, total hysterectomy is the preferred routine procedure if for no other reason than to prevent the subsequent development of carcinoma of the cervical stump.

The value of postoperative radiation has been discussed at length in the literature, with wide divergence of opinion. The authors believe that it should be administered to all patients with tumors of high-grade histologic malignancy (serous carcinomas of Grade II and III and the undifferentiated and unclassifiable carcinomas) even if localized to the ovaries. It seems of no

value in tumors of low-grade histologic malignancy (papillary serous cystadenocarcinoma, borderline and Grade I; most papillary pseudomucinous cystadenocarcinomas; most granulosa-cell tumors) unless there is operative evidence of spread beyond the ovaries; in the latter event, x-ray therapy is indicated. It should be given to all patients with extension of tumor beyond the ovaries regardless of the amount of spread and regardless of the histologic type.

The future must offer more than early clinical diagnosis if ovarian cancer survival is to be materially increased. Perhaps this will be a method affording early histologic or cytologic diagnosis that will precede clinical signs; perhaps it will be higher-voltage x-rays or improved methods of administering radiation.

Six charts; 8 tables. ROBERT H. LEAMING, M.D.  
Jefferson Medical College

**Testicular Tumor and the Status of Radiation Therapy.** Melville L. Jacobs. *Urol. & Cutan. Rev.* **53:** 599-601, October 1949.

The author has traced in chronological order the various forms of treatment of tumors of the testicle in an attempt to evaluate them and to determine the place of irradiation.

In summarizing and comparing results he found four- and five-year survival rates for simple orchiectomy to be only 6 per cent. For radical surgical intervention they range from 5.6 to 24 per cent. The average five-year survival rate for simple orchiectomy plus irradiation was found to be 47.19 per cent. The superiority of this method over surgery, simple or radical, is apparent.

In 1932, Randall and Pancoast and in 1940 Randall and Chamberlin (*Tr. Am. A. Genito-Urin. Surgeons* **33:** 297, 1941) used preoperative irradiation for testicular tumors. In Randall and Pancoast's series of 12 patients treated with preoperative irradiation 11 were alive and well after eight years. Randall and Chamberlin reviewed 45 cases given preoperative irradiation and found 91 per cent living and well two years after treatment. In a similar group of cases given postoperative x-ray treatment only 56 per cent were alive and well after two years. These authors believed their figures to be justification for preoperative irradiation followed in four to six weeks by simple orchiectomy.

There have been many objections voiced to the use of preoperative x-ray therapy, chief of which is that it is difficult to make a satisfactory microscopic diagnosis in a tumor which has been heavily irradiated.

The value of irradiation in treating testicular tumors is established. Its preoperative use has not as yet been evaluated. It is hoped that it may be given an adequate trial.

HUGH A. O'NEILL, M.D.  
Cleveland, Ohio

**Radium in Treatment of Hemangioma.** F. Ronchese. *Arch. Dermat. & Syph.* **60:** 717-721, November 1949.

The author believes that the majority of infantile hemangiomas disappear spontaneously within four or five years and that, if size, location, sex, and parents' cooperation justify expectant therapy, this is the line of choice. If the hemangioma is large and cavernous or small and easily removable, or if it is on an exposed part and the parents are unwilling to wait four or five years for a spontaneous involution, the form of active treatment considered the best should be administered.

In 347 miscellaneous hemangiomas seen by the author in the last fifteen years, 89 were treated with surface radium and 5 with radon implants. The surface radium was in the form of the usual tubes of 25 or 50 mg. each, the container representing a filtration of 0.5 mm. of silver and 1 mm. of brass, held at 1 cm. distance from the skin for three to four hours, at intervals of six to eight weeks, from one to ten times, the hemangioma being surrounded by 1 mm. of lead foil.

Re-examination of 28 cases of infantile cavernous hemangioma treated with radiations ten to fifteen years previous to this study failed to show any cutaneous, bony or articular sequelae.

In the author's opinion, between the "all-for-radium" attitude of some years ago and the present trend of condemnation there lies a happy medium, and treatment should be suited to the individual case.

Five photographs.

**Cavernous Haemangioma of the Perineum.** Nicholas Alders. *J. Obst. & Gynaec. Brit. Emp.* 56: 1038-1040, December 1949.

A case of cavernous hemangioma with superimposed papillomata of the perineum in a 55-year-old female patient is described. The papillomata were removed with the diathermy knife, and the hemangioma was treated with roentgen rays, with satisfactory results.

One photograph; 1 table.

MORTIMER R. CAMIEL, M.D.  
Brooklyn, N. Y.

**Radioresistant Hemangiomas.** Juraj Körbler. *Radiol. clin.* 18: 392-397, November 1949. (In German)

The great majority of hemangiomas are radiosensitive. There are some, however, which do not respond to radiation. The author emphasizes that a biopsy is not a sufficient criterion of the radiosensitivity of hemangiomas. The classification of these lesions from the histopathological standpoint alone is unsatisfactory. Two cases are cited in support of this contention.

The first case is that of a 12-year-old boy with a hemangioma on the posterior portion of the leg, which was treated with radium, 2,975 mg. hr., with 1.5 mm. Pt filtration, at a distance of 2 cm. The histologic diagnosis was hemangioma simplex. Two years later, the lesion was larger and biopsy revealed no change.

The second patient, a 20-year-old male, was treated three times with radium at three-month intervals, for a hemangioma on the dorsal surface of the right foot: 4,008 mg. hr. were given the first time with 1 mm. Pt, at 1 cm. distance; 3,320 mg. hr. were given the second time, and 3,800 the third time, with the same filtration and distance. The hemangioma did not regress, and no histologic changes were observed even after these heavy dosages.

One photograph. EUGENE F. LUTTERBECK, M.D.  
Cook County Hospital, Chicago

**Eosinophilic Granuloma of the Skin.** Edward A. Oliver, James R. Webster, Julius E. Ginsberg, and H. S. Steinberg. *Arch. Dermat. & Syph.* 60: 701-713, November 1949.

Two cases are reported, presenting entirely different clinical characteristics but with histologic findings thought to be compatible with a diagnosis of eosinophilic granuloma of the skin.

One patient exhibited a generalized eruption, and

during the course of his illness the signs of Loeffler's syndrome developed. A decided leukocytosis was continually present, with an eosinophil count as high as 66 per cent. Under roentgen irradiation directed toward the main concentrations of the reticulo-endothelial system, the patient began to show improvement; after completion of the course of irradiation, all cutaneous lesions disappeared and in a short time the blood count returned to normal. When the patient was last seen, almost a year after discharge from the hospital, his skin was clear, blood counts were within normal limits, and roentgenograms of the chest showed no pathologic changes. Treatment was given in this case to eight fields over the pelvis and upper abdomen. The fields were treated in rotation until each had received 600 r. Only one field was treated daily and none received treatment oftener than every ten days. The daily dose was 150 r (140 kv.; 0.5 mm. copper filter; 20 ma.; time 8.5 minutes).

The second patient had slowly developing dark, cherry red, plaque-like lesions on the face. Eight treatments of 75 r each at weekly intervals were administered while he was in the Navy, but at the time of the report, about five years later, his condition was unchanged.

Six illustrations.

**Extramedullary Plasmocytomas.** Poul E. Andersen. *Acta radiol.* 32: 365-374, Dec. 31, 1949.

About 200 cases of extramedullary plasmocytoma have now been reported in the literature. They usually occur in men between forty and seventy. The most frequent sites are the upper air passages, oral cavity, and conjunctiva, though numerous other locations have been recorded.

Histologically there are three groups of extramedullary plasma-cell tumors: (1) granulomatous tumors or chronic inflammatory conditions (granuloma plasmacellulare) (2) plasmocytomas very closely resembling Hodgkin's disease, (3) the true extramedullary plasmocytomas which the author feels are sometimes benign but more often malignant.

The true extramedullary plasmocytomas are ordinarily seen in the upper air passages, oral cavity, cervical lymph nodes, and intestines. They may be solitary, multiple, or generalized, and they spread first to regional lymph nodes, usually with involvement of bones later.

Granuloma plasmacellulare, the first histologic group, is most frequently seen in the conjunctiva and is often preceded by trachoma. This granuloma has been found in most other organs and regions, especially the upper air passages.

Treatment is usually surgery, sometimes followed by radiotherapy. Interstitial radium seems to be of special value. Five-year survivals without recurrence are few if the conjunctival plasmocytomas are excluded. The remainder must be considered then as very malignant, regardless of the histologic picture.

Eight new cases are presented. One case each was noted in the cervix and testes, areas not previously mentioned in the literature. R. C. DATZMAN, M.D.  
Indiana University

**Roentgen Therapy of Thrombophlebitis.** Claude R. Sneed, Jack Lasner, E. L. Jenkinson, and Geza de Takats. *J. A. M. A.* 141: 967-969, Dec. 3, 1949.

A selected group of patients with thrombophlebitis of the extremities has been exposed to roentgen therapy.

One hundred consecutive cases are reported. The patients are classified in six clinical groups: (1) acute superficial phlebitis in persisting varicosities; (2) acute superficial phlebitis in veins collateral to deep venous obstruction; (3) migrating phlebitis of thromboangiitis obliterans (Buerger's disease); (4) deep venous thrombosis of the calf; (5) iliofemoral venous thrombosis; (6) subacute thrombophlebitic indurations.

Treatment factors are 200 kv., 1.9 mm. Cu h.v.l., focal skin distance 50 cm. The number and size of the fields vary. An area of 400 sq. cm. or less is treated each day with a dose of 80 r (in air). The interval between consecutive treatments is two to seven days. One to six treatments may be given, most patients requiring one to three treatments to each area. No skin reaction, damage to tissue, or irradiation sickness has been noted with this dosage. Severe febrile reactions have been seen with doses of 150 to 200 r. The optimal dose for most acute and subacute lesions seems to be 80 to 100 r. It seems wise to allow the reaction to subside before the next dose is given.

Treatment was considered successful when periphlebitic exudate subsided, when pain was relieved, and when ambulation was possible. This occurred in 85 of 100 patients treated. The result was described as doubtful if the response was not immediate or if the improvement could have been attributed to other forms of therapy. Nine cases came under this category. There were 6 failures. The clinical type of thrombophlebitis is apparently not related to the response to irradiation.

The object of treatment is to hasten the absorption of inflammatory exudate and to overcome blockade of lymph at isthmus points, such as the popliteal fossa, the groin, and axilla. The dissolution of lymphocytes may raise the level of gamma globulin in the blood and increase the titer of antibodies. Other possible mechanisms are mentioned. Roentgen therapy does not seem to affect the thrombus *per se* or the sympathetic nervous system but, by hastening absorption of the periphlebitic exudate about the adventitia of the vessels, relieves pain and reflex vasospasm. The thrombus itself requires other forms of therapy, such as the administration of anticoagulants, division of veins, or the use of sympathetic block.

One table.

M. M. FIGLEY, M.D.  
University of Michigan

**Effect of Preoperative Roentgen-Ray Therapy on Arterial Hypertension in Embryoma (Kidney).** J. Edmund Bradley and Miles E. Drake. *J. Pediat.* 35: 710-714, December 1949.

Arterial hypertension is associated with embryoma of the kidney in from 77.9 per cent to 93.8 per cent of the

recorded cases. The authors report 10 cases which were treated with roentgen irradiation preoperatively. Four of these patients had a marked fall in blood pressure five to eight days after the beginning of treatment. Three of the 4 had a reduction in the size of the tumor, but this was preceded in all cases by the change in blood pressure. The other 6 patients did not respond with any lowering of the blood pressure or diminution in the size of the tumor five to eight days after beginning treatment.

One chart; 1 table.

HOWARD L. STEINBACH, M.D.  
University of California

**Wide Field Irradiation and the Platelet Count.** W. M. Court Brown. *Acta radiol.* 32: 407-427, Dec. 31, 1949.

Wide-field irradiation has been used at the Royal Infirmary, Edinburgh, Scotland, increasingly since 1942 for palliation of the reticuloses and in the treatment of very radiosensitive tumors. In this connection the white blood count has not proved an entirely satisfactory form of control. In a few cases severe and fatal anemia has developed, with petechial hemorrhages, though the white blood count remained satisfactory. A study was therefore undertaken of the platelet count, and this has been found to yield valuable information in the guidance of treatment.

Cases with normal hemopoiesis show an average range of 200,000 to 400,000 platelets per cubic millimeter. Daily counts in patients undergoing wide-field irradiation showed peak values of 105 per cent to 252 per cent in the first two weeks of therapy, followed by a steady fall that is related to the field size. A safety level of 100,000 platelets per cubic millimeter has been determined by experience.

In cases of impaired hemopoiesis, usually resulting from previous irradiation, response was altered quantitatively rather than qualitatively. It was frequently found that these patients had a normal white cell and lymphocyte count. A comparison of the accepted safety levels of 2,000 white cells and 300 lymphocytes with that of 100,000 platelets showed that cases with a safe platelet level not infrequently fell below the other standards, but recovery ensued. Conversely radiation anemia supervened with lymphocyte and white cell counts considerably above the safety level.

The author emphasizes consistency in technic of platelet count and in the time of treatment and the time at which the count is performed. One technician must do all the counts on one patient.

Six case histories are given. Seventeen charts.

DAVID C. GASTINEAU, M.D.  
Indiana University

## RADIOISOTOPES

**Radioiodine Uptake Curve in Humans. II. Studies in Children.** George H. Lowrey, William H. Beierwalter, Isadore Lampe, and Henry J. Gomberg. *Pediatrics* 4: 627-633, November 1949.

Twenty-six children ranging from one month to fourteen years of age were given 20 to 50 microcuries of radioiodine orally, after which measurements of the thyroid uptake were made at intervals during the first two hours and, when possible, at twenty-four and forty-eight hours. A Geiger-Müller counter shielded to regis-

ter only gamma rays was used and was placed against the gland parallel with the isthmus.

The series included 12 normal children, all of whom showed a progressive uptake of iodine which by two hours had exceeded the base line count taken at ten minutes by 125 to 400 per cent. A continued increase was observed at the twenty-four- and forty-eight-hour readings.

The 14 remaining patients had various illnesses and showed the following results:

1. Normal curves were obtained on a patient with rheumatic fever and on another patient with nephrosis.

2. Two patients with colloid goiter had an increased iodine uptake exceeding the normal range. In one of these, radioiodine studies made after two months of Lugol's solution medication showed a much lower pick-up than repeat studies after the Lugol's solution was withheld.

3. In one child with hyperthyroidism the radioiodine uptake exceeded the base-line count by 2,000 per cent in one hour.

4. The remaining 9 patients were considered examples of thyroid hypofunction and had a low iodine uptake. Four cretins, one child with juvenile myxedema, and one with Hurler's syndrome (gargoylism) showed values of less than 40 per cent at all times. Despite some variation from this typical hypothyroid curve, a low iodine uptake was also obtained in one pituitary dwarf, one mongolian idiot, and one case of hypothalamic syndrome.

The procedure described is valuable in estimating thyroid function and appears more specific than methods in present use. A certain degree of overlapping in the radioiodine uptake curves obtained on normal and abnormal subjects can occur.

Two charts.

CORNELIUS COLANGELO, M.D.  
Chicago, Ill.

**Treatment of Metastatic Thyroid Cancer with Radioactive Iodine: Credits and Debits.** J. B. Trunnell, L. D. Marinelli, B. J. Duffy, Jr., Ruth Hill, Wendell Peacock, and Rulon W. Rawson. *J. Clin. Endocrinol.* 9: 1138-1152, November 1949.

This study included 25 patients with distant metastases from carcinoma of the thyroid. On the credit side were the following observations: 1. Demonstration that ablation of the normal thyroid tissue by surgery or large doses of radioiodine was followed by increased uptake of radioiodine ( $I^{131}$ ) by the metastases. A similar increase in the ability of the metastases to concentrate radioiodine was noted in thyroidectomized patients receiving treatment for several weeks with thyroid-stimulating hormone or thiouracil. 2. Clinical improvement in 4 of 9 patients with "functional" metastatic cancer receiving cumulative doses varying from 145 millicuries to 906 millicuries. The tumors shrank or showed histologic changes of destruction, but viable cancer was present in all at the time of this report.

The study yielded the following observations of an undesirable nature. 1. In 3 patients who had received large doses of  $I^{131}$  for the purpose of destroying the normal thyroid or functioning metastases, hyperthyroidism developed within two weeks after treatment. 2. In 3 females with previously normal menstrual cycles amenorrhea and hot flashes followed cumulative doses of 90 to 458 millicuries which produced total blood radiation estimated as equivalent to 200, 400, and 450 roentgens. 3. The most serious unfavorable change was a depression of hematopoiesis in the 9 patients receiving therapeutic doses of radioiodine. This was revealed by lymphopenia, thrombocytopenia, and reversal of the erythroid-myeloid ratio in the bone marrow.

In patients receiving lower radiation doses to the blood, the marrow recovered in four to six months, but in one patient receiving a total dose of 638 millicuries of  $I^{131}$ , fatal pancytopenia developed. The estimated

blood radiation in this case was 1,300 equivalent roentgens.

Eleven illustrations, including 1 roentgenogram.

CORNELIUS COLANGELO, M.D.  
Chicago, Ill.

**The Function of Various Types of Thyroid Carcinoma as Revealed by the Radioautographic Demonstration of Radioactive Iodine ( $I^{131}$ ).** Patrick J. Fitzgerald and Frank W. Foote, Jr. *J. Clin. Endocrinol.* 9: 1153-1170, November 1949.

This paper presents the information obtained from 100 specimens of thyroid carcinoma studied by radioautographs. In most of the cases small "tracer" doses, 0.3 to 5 millicuries, were given, while the rest received large therapeutic doses. While radioautographic techniques differ, the principle is to expose a radiosensitive emulsion by placing it in contact with a section of the isotope-containing tissue. The radioautograph represents the concentration and distribution of the isotope in the tissue and can be correlated with its histologic appearance.

Radioiodine shows a selective affinity for normal thyroid follicles. Because of this, any treatment of thyroid carcinoma necessitates removal of the gland or inhibition of its functioning tissue, so that the malignant lesions, both primary and metastatic, have the opportunity to pick up the isotope.

The more closely thyroid carcinoma resembles the normal follicular pattern, the more likely it is to concentrate radioiodine. In addition, the more colloid present, the greater the uptake of iodine. The problem of  $I^{131}$  dosage, however, is not a simple one, since in the normal gland, adjacent follicles show wide variations in iodine uptake, suggesting a periodic or intermittent ability to concentrate this substance. Historadiography reveals the over-all amount of atomic iodine present in the follicle and may be used in combination with radioautographs to show what fraction of this total iodine is present as  $I^{131}$ , *i.e.*, to demonstrate the metabolism of iodine by the follicle under study. As yet, tissue dosage by radioiodine is complex, and dosage calculations are inexact. It is estimated that 0.2 microcuries of  $I^{131}$  per gram of thyroid is adequate concentration for radioautography, but until microdensitometric analysis of radioautographs becomes practical, tissue doses cannot be estimated by this method.

Of the 100 carcinomas studied, 46 showed radioautographic evidence of concentration of the isotope, and in almost every instance the tumor showed a resemblance to normal thyroid in respect to the presence of follicles or colloid. The papillary type, which represents about 50 per cent of all thyroid carcinomas, is the least malignant; concentration of iodine was obtained in 28 per cent of this group. The alveolar and follicular type, which is next in the order of malignancy, concentrated  $I^{131}$  in 75 per cent of the cases studied, but this group represents only 10 per cent of all thyroid carcinomas. The resemblance of this type of carcinoma to normal functioning thyroid explains the high percentage of cases picking up radioiodine. The solid cellular type of carcinoma makes up 20 per cent of all thyroid cancer; 5 out of 12 of these concentrated  $I^{131}$  (42 per cent). Hürthle-cell carcinomas represent 10 per cent of all thyroid cancer; of 9 of these, 3 (33 per cent) showed  $I^{131}$  pick-up but of such a sparse nature as to make the radioautograph of little value. Spindle- and giant-cell

carcinoma and anaplastic carcinoma constitute 15 per cent of all thyroid carcinomas and are the most malignant types. Of 13 cases studied, none concentrated radioiodine.

Nine illustrations; 2 tables.

CORNELIUS COLANGELO, M.D.  
Chicago, Ill.

**Method for the Preoperative Estimation of Function in Thyroid Tumors: Its Significance in Diagnosis and Treatment.** Brown M. Dobyns, Bengt Skanse, and Farabe Maloof. *J. Clin. Endocrinol.* 9: 1171-1184, November 1949.

A Geiger-Müller counter with a small window was used as a means of preoperatively determining the relative function of thyroid nodules. Counts were made over the thyroid forty-eight hours after administering a tracer dose of radioiodine in 41 cases of nodular goiter, and the accuracy of the method was checked by radiographs obtained after the removal of the gland.

The counter method showed increased radioactivity over hyperfunctioning nodules. When reduced radioactivity was found over a nodule, a malignant lesion was suspected, since carcinoma is known to concentrate radioiodine poorly. The importance of this finding is obvious when one recalls that 20 per cent of all solitary nodular goiters are found at operation to be malignant.

Thyrotoxicosis from a hyperfunctioning nodule gave evidence of a localized increase in radioactivity; thyrotoxicosis from a diffuse hyperfunctioning of the gland (Graves' disease) gave a uniform increase in radioactivity over the entire gland.

The accuracy of the counter technic was influenced by: (1) the varying depth of the gland, (2) the position of the nodule, (3) the presence of multiple nodules, (4) necrosis in hyperfunctioning nodules, (5) the presence of small nodules in which detection of hypofunction was difficult.

Seven illustrations; 1 table.

CORNELIUS COLANGELO, M.D.  
Chicago, Ill.

**Radioiodine Therapy of Metastases from Carcinoma of the Thyroid: A Six-Year Progress Report.** S. M. Seidlin, I. Rossman, E. Oshry, and E. Siegel. *J. Clin. Endocrinol.* 9: 1122-1137, November 1949.

Twelve cases of metastatic thyroid carcinoma were treated in the following manner: Uptake of radioiodine ( $I^{131}$ ) by the metastases was induced, when necessary, by surgical or radiation thyroidectomy or by injections of thyroid-stimulating hormone and was confirmed by tracer studies, after which multiple large doses of the isotope—100 millicuries or more—were given. The total dose ranged from about 200 to about 1,000 millicuries.

Seven patients were alive at the time of the report, from five months to six years after the initiation of therapy, of whom 3 were greatly improved, 2 improved, and 2 unimproved. Of the 5 who died, 3 showed initial improvement for periods ranging from one to three and one-half years.

In general, the more differentiated the tumor, the greater was its ability to take up radioiodine, but exceptions were noted. The radiation delivered to the tumor depended upon the concentration and distribution of the isotope within the tumor rather than upon the amount administered.

Details of one case on which earlier reports have appeared (see *J. A. M. A.* 132: 838, 1946. *Abst. in Radiology* 49: 657, 1947), now followed for six years, are given. A skull metastasis recently excised from this patient showed absence of viable tumor cells, and a residual necrotic debris which bore no resemblance to the pre-irradiation histologic appearance. It was found, however, that this necrotic debris could still concentrate radioiodine.

Ten figures; 1 table.

CORNELIUS COLANGELO, M.D.  
Chicago, Ill.

**Effect of Thyroid Secretory Activity on the Distribution of Radioiodine in Plasma.** Albert M. Potts, Reginald A. Shipley, John P. Storaasli, and Hymer L. Friedell. *J. Lab. & Clin. Med.* 34: 1520-1525, November 1949.

The activity of the thyroid gland determines three things with respect to iodine: (1) the rate at which inorganic iodine is removed from the blood; (2) the amount of iodine retained by the gland; (3) the rate at which the hormone, containing organic iodine, is released into the blood.

With these premises in mind, a tracer dose of radioiodine,  $I^{131}$ , was given by mouth to 13 patients with hyperthyroidism, 11 normal subjects, and 5 patients with myxedema, after which radioactive determinations (with a Geiger-Müller counter) were made on both the inorganic and organic iodine fractions of plasma samples drawn at two, eight, and twenty-four hours. These readings showed that the inorganic iodine of the blood declines more rapidly in hyperthyroidism than in normal states, while in myxedema the decline tends to be slower than normal. These findings reflect an increased (inorganic) iodine uptake in hyperthyroidism and a reduced iodine uptake in myxedema.

Plasma determinations carried out on the organic hormonal iodine showed an elevation in all types of cases at the end of two hours, followed by a decline in normal and myxedematous subjects which progressed between the eighth and twenty-fourth hours. By contrast, a marked elevation was noted in hyperthyroid subjects between the eighth and the twenty-fourth hours. These findings are again a reflection of the hyperactivity of the gland in hyperthyroidism, and of the relatively reduced thyroid activity in normal and hypothyroid states.

One chart; 1 table. CORNELIUS COLANGELO, M.D.  
Chicago, Ill.

**Iron Metabolism. Erythrocyte Iron Turnover.** C. A. Finch, J. A. Wolff, C. E. Rath, and R. G. Fluharty. *J. Lab. & Clin. Med.* 34: 1480-1490, November 1949.

The authors investigated the erythrocyte unit of metabolism by using patients and animals who had enlarged iron stores and/or bone marrow dysfunction, since these conditions block the re-utilization of radioactive iron released by broken-down red cells. Thus the fate of tagged cells was observed as an isolated phenomenon, and it was possible to measure the life span of a red cell population of a single age. Observations were made on tagged macrocytes, microcytes, and normal red cells in normal and anemic recipients (of blood transfusions). It was noted that the reticulocytes from a patient with pernicious anemia responding to therapy

had a relatively normal life span, as did those of a patient with an iron deficiency.

The daily turnover of erythrocyte iron in man and dog was found to be 1 per cent.

There is no discernible exchange of iron between the

erythrocyte and its surroundings throughout its life span.

Five illustrations; 1 table.

CORNELIUS COLANGELO, M.D.  
Chicago, Ill.

## RADIATION EFFECTS

**Discussion on the Physical, Cytological and Medical Aspects of Protection from Ionizing Radiations with Special Reference to the Use of High-Voltage X-Rays and Radio-Isotopes.** Katherine Williams and W. G. Marley. *Proc. Roy. Soc. Med.* 42: 923-934, November 1949.

Williams points out that protective measures must keep in step with the recent rapid progress in nuclear physics consisting in the development of piles, cyclotrons, betatrons, and other high-energy generators, together with the increasing availability of radioactive isotopes. These developments have increased the potential hazards to health from radiations and radioactive substances, including active dusts and gases. For high-voltage x-rays or other high-energy radiation the protective measures differ quantitatively rather than qualitatively from those with less powerful machines. Distance and shielding are the two most important factors. The extremely small amounts of radioactive dust and gases which are permissible in the air of a room call for ventilating systems of high efficiency.

Distance is the best and easiest form of protection. As to shielding, the gamma radiation from most isotopes will be absorbed by about 2 inches of lead in the majority of cases. Good laboratory housekeeping is essential, and constant checking of conditions is necessary. The monitoring should be continual.

The maintenance of the health of the workers is the final and acid test of the efficiency of the planning procedures and working conditions. The normal base line of the health of the individual worker must be established, so that any significant deviation can be noted. This can be done by using pre-employment or pre-exposure medical examinations, to include a full history, personal and occupational, history of previous radiation exposure, including screening for diagnostic purposes, clinical examination, blood count, and chest roentgenography. The condition of the skin, nails, and eyes should be noted. Hematologically, a base line may be established by taking 2 or 3 counts several days apart before exposure, at the same time of day.

Physical methods of achieving protection from high-energy radiation and radioactive isotopes is discussed by Marley. He states that in any laboratory where high-energy radiation or radioactive isotopes are used, it is desirable that one person, usually a physicist, should be made responsible for all protection arrangements and that he should work in close collaboration with a qualified medical advisor. Adequate radiation hazard control of a large establishment involves a wide range of technology and extensive organization. The precautions are expensive, but perhaps not nearly so expensive as the consequences of failure.

For external irradiation, the Protection Subcommittee of the British Medical Research Council recommended in 1948 the adoption of 0.5 r per week as the maximum permissible exposure to x or gamma radiation which may be continued over an indefinite period. In work with radioactive isotopes, no tissue or organ

of the body should accordingly receive more than this or the equivalent quantity, 0.5 rep of beta radiation in one week, except for the hand, which may receive up to 1.5 rep per week. It has been recommended that the tolerance for alpha particles should be 1/10 of the 0.5 rep per week, to allow for the higher specific ionization along the particle tracks and the increase in damage produced. It appears that the maximum permissible dose of neutrons received in one week should not exceed about 1/20 of that for x and gamma rays when measured physically (*i.e.*, in rep).

It is generally agreed that, for persons subject to monitoring control, the maximum permissible body burden of radium taken internally is 0.1 microgram. The maximum permissible human body burden of Sr<sup>90</sup> is probably about 1 microcurie. From these basic data it is possible to compute tolerances for a number of similar isotopes and equivalent quantities for other isotopes can be computed in a similar way, taking into account the nature of the radiation and metabolic processes, such as absorption, excretion, location, and translocation in the body.

The authors present considerations in personnel monitoring, area monitoring, and air-contamination monitoring. The specific hazards in physics and chemistry areas are considered in detail, and the authors comment upon methods of disposal of active waste.

Four illustrations.

E. S. KERESKES, M.D.  
University of Arkansas

### Early Reactions Following Roentgen Ray Epilations.

I. Zugerman. *Arch. Dermat. & Syph.* 60: 722-725, November 1949.

A study was made of 312 children to determine the cause of early reactions (restlessness, nausea and vomiting, headache, loss of appetite, and elevation of temperature) following roentgen epilation for ringworm of the scalp. The total group was divided into quiet, co-operative children and nervous, restless ones in order to determine whether nervousness is a factor in the reactions. The patients were further divided into 7 groups, which were treated with rays of different quality, depending on the voltage and inherent filtration of the tubes. The technic described by MacKee and Cipollaro was used.

It was found that in nervous, unco-operative children there is a substantially higher percentage of reactions and a tendency to greater severity. Higher voltages and filtrations also increased the incidence and severity of the reactions. The author believes a low voltage, not in excess of 80 kv., and low filtration, not to exceed a half value layer of 0.5 mm. aluminum, should be employed in the treatment of ringworm.

**Malignant Degeneration of Benign Giant Cell Tumor of Bone.** T. Leucutia and James C. Cook. *Am. J. Roentgenol.* 62: 685-706, November 1949.

The authors studied 77 cases of benign giant-cell tumor of bone which were treated at Harper Hospital,

Detroit, between the years 1923 and 1947. Seven of these (9 per cent) underwent malignant change and these cases are presented in detail. In 4 the malignant change followed routine roentgen therapy, in 1 it was apparently spontaneous, and in 2 it followed surgery.

The authors also present a rather extensive review of cases reported in the literature. Their conclusion is that "the malignant degeneration of the giant-cell tumor of bone occurs in a limited number of cases (10 to 15 per cent) as a natural sequence of events unaffected by the type of treatment given."

Forty-seven roentgenograms; 1 photograph; 11 photomicrographs.

J. B. SCRUGGS, M.D.  
University of Arkansas

**Radiodermatitis and Necrosis.** Thomas D. Cronin and Raymond O. Brauer. *Surgery* 26: 665-672, October 1949.

Despite our increasing knowledge of tissue tolerance to ionizing radiation and the accuracy with which modern equipment can deliver a measured dose, radiodermatitis and necrosis are still seen too frequently. These lesions are classified into three groups.

**Group I:** Lesions resulting from a single massive dose, intentional or otherwise, or from a few exposures at short intervals. Many patients in this group had been subjected to prolonged fluoroscopy; others to accidentally prolonged x-ray therapy or to a few excessive doses.

**Group II:** Lesions due to many exposures over a long period of time, usually in the treatment of various benign skin conditions. Frequently the patient was guilty of "shopping around" and denied previous x-ray therapy.

**Group III:** Lesions in professional roentgenologists. An important factor in the production of radiodermatitis in this group is the latent period, together with the fact that repeated doses have a cumulative effect.

The authors have seen 30 patient of Group I, 21 of Group II, and 3 of Group III. They consider radiation burns justified only in those cases of malignant neoplasm in which radiation therapy is the treatment of choice. Excluding the cases in Group III, there were only 7 cases out of 51 in which the skin changes would be justified because of the gravity of the original condition.

Chronic radiodermatitis consists in hypertrophy of the epithelium, atrophy of the corium, and loss of the sebaceous glands, hair follicles, and sweat glands, in that order. There is a marked obliterative endarteritis affecting all vessels and seriously reducing the blood supply to the area. The skin has an atrophic, tight, dry appearance, with many telangiectatic vessels. Keratoses are common, and small ulcerations may occur, which heal slowly.

Pain is an outstanding feature of all deep burns. It is usually a late occurrence, but where massive doses have been given in a short time pain may develop within a few days. Itching, burning and dryness are characteristic where the dermatitis is due to small doses of radiation repeated over many years. Carcinoma seems more likely to develop in those patients who have received small repeated doses.

Treatment consists in either palliation or complete surgical removal of all diseased tissue. Palliative treatment is of value only in (1) acute ulcerations, (2) for symptomatic relief of early or mild radiodermatitis, (3) where surgery is refused or cannot be performed. For the palliation of acute ulcerations, a moist dressing of saline or boric solutions, soothing ointments and lotions,

and aloe vera leaves have all been useful. Radon ointment has been used by some.

Most lesions of any size are purely surgical problems, calling for complete excision or desiccation. Excision and primary closure are indicated whenever possible, but most cases are rather extensive and skin grafting is necessary. Split-skin grafts may be used where there has not been severe damage to the deeper structures; otherwise pedicle grafts are necessary. Amputation is indicated in an extremity where radiodermatitis has become malignant and invaded deeper structures.

Seven photographs. ALFRED O. MILLER, M.D.  
Louisville, Ky.

**Pregnancy Following Pelvic Irradiation.** Alan M. Giles. *J. Obst. & Gynaec. Brit. Emp.* 56: 1041-1043, December 1949.

The author believes that: (1) intra-uterine sterilizing doses of radium are not justifiable unless steps are taken to prevent subsequent pregnancy; (2) that if radium is used, a big enough dose should be given to ensure an effective menopause; (3) that induction of the menopause by this method in women under forty is hazardous; (4) that patients treated thus should be followed for at least twelve months, and failure to produce the menopause should be considered an indication for contraceptive measures.

Two 32-year-old women were given intra-uterine radium. One received a dose of 2,400 mg. hr. and the other 1,000 mg. hr. After a varying interval, each began to menstruate again, and in each case pregnancy was followed by spontaneous abortion of a macerated fetus. The second patient had a subsequent pregnancy, which was complicated by prolonged labor due to rigidity of the cervix and resulted in a stillbirth.

MORTIMER R. CAMIEL, M.D.  
Brooklyn, N. Y.

**Effect of Spleen Protection on Mortality Following X-Irradiation.** L. O. Jacobson, E. K. Marks, M. J. Robson, E. Gaston, and R. E. Zirkle. *J. Lab. & Clin. Med.* 34: 1538-1543, November 1949.

The lethal dose of total-body irradiation for mice whose spleens were protected was almost twice that for animals whose spleens were included in the exposure. Thus the dose required to kill half of a given group of mice observed for a twenty-eight-day period (LD 50) was less than 600 r when the spleen was unprotected and was 975 r when the spleen was protected. Factors were 240 kv. and a half-value layer of 1.0 mm. copper.

The beneficial effect of the spleen in reducing the lethal effect of total irradiation is not fully known, but two mechanisms are suggested: (1) It compensates for the destruction of hematopoietic tissue elsewhere in the body. (2) It plays a role in the formation of an anti-hemolytic antibody.

One chart; 1 table. CORNELIUS COLANGELO, M.D.  
Chicago, Ill.

**Influence of Estrogens on the Acute X-Irradiation Syndrome.** H. M. Patt, R. L. Straube, E. B. Tyree, M. N. Swift, and D. E. Smith. *Am. J. Physiol.* 159: 269-280, Nov. 1, 1949.

Experiments carried out by the authors confirm the observation of Treadwell and her co-workers (*Endocrinology* 32: 161, 1943) that pretreatment with estradiol benzoate improves the survival of male mice after

lethal x-irradiation. It is demonstrated further that the estrogen protective effect occurs in female mice as well and that benzestrol, but not progesterone and testosterone, is also effective. The time of injection of estrogen relative to the time of irradiation is critical, for estradiol is most effective when it is given ten days before the exposure. Estradiol in dosage sufficient to protect against x-rays does not influence survival after poisoning with a nitrogen mustard.

It was found that estradiol increased adrenal weight and accelerated thymic involution but had no appreciable effect on the weight of the spleen, inguinal nodes, or kidneys. Although the increase in adrenal weight after x-irradiation was somewhat greater in mice pretreated with estrogen, the radiation-induced involution of spleen, thymus, and inguinal nodes was not altered.

A leukopenia with maximal depression around ten to fourteen days after estrogen injection was observed. The reduction in heterophils was more marked and somewhat more consistent than the lymphocyte response. Little change was noted in the erythrocyte count following the single injection of estradiol. Leukocytes were decreased to the same levels in both the estrogen-treated and control irradiated animals, although maximal depression and recovery occurred earlier in the former. The more rapid recovery of leukocytes in irradiated mice that received a prior injection of estrogen resides in the heterophil component. The anemia of radiation was also less severe in the estrogen-treated animals. Significantly, the maximal estrogen protective effect is observed when mice are irradiated during their leukopenic period. That there is some correlation between heterophil response and lethal effect is indicated by the finding that a rapid recovery of heterophils but not of lymphocytes occurs in mice treated with estradiol ten days before x-irradiation. The possibility is considered that estrogen stimulation renders myelopoietic tissue more resistant to x-rays, perhaps because these tissues are in a proliferative phase during or shortly after the irradiation.

Eight charts; 5 tables.

**Fluorescein as an Adjunct in the Treatment of Radionecrotic Ulcers.** Bromley S. Freeman. *Surg., Gynec. & Obst.* 89: 566-569, November 1949.

The author gives a brief review of the treatment of ulcers due to radiation therapy. In determining the vascularity of tissue in the region of an ulcer, fluorescein has been given intravenously and the ulcerated area then viewed in ultraviolet light. Fluorescein appears in the viable tissue and fluorescence of this compound occurs in ultraviolet light. This is of particular value to the surgeon in treating radionecrotic ulcers, as the extent of necrosis can be more easily determined in this manner than by the conventional methods.

Five illustrations. HENRY C. BLOUNT, JR., M.D.  
University of Pennsylvania

**Hematologic Studies in Hiroshima and a Control City Two Years After the Atomic Bombing.** Fred M. Snell, James V. Neel, and K. Ishibashi. *Arch. Int. Med.* 84: 569-604, October 1949.

The authors attempt to answer the question: What

was the peripheral hematologic picture twenty to thirty-three months after the atomic bombing of Hiroshima, in persons who received large amounts of whole body radiation?

The criterion adopted for the selection of relatively heavily irradiated subjects was the occurrence of scalp epilation. Epilated subjects were selected at random; the majority were school children.

A control population comparable in age, sex, nutritional status, and occupation was studied in the city of Kure, which is located some 18 miles from Hiroshima. In Hiroshima, 924 persons were examined; in Kure, 935.

Each person selected for study was given a brief physical examination; as many of the following blood values as circumstances permitted were then determined; erythrocyte and leukocyte counts, differential blood count, hemoglobin concentration, hematocrit reading, plasma protein level, and, for a smaller number of persons, reticulocyte count. Results are compared not only in terms of the mean values for the two populations but also in terms of the mean differences between randomly established pairs of similar control and epilated individual subjects.

The irradiated subjects of this study appear for the most part to have made a complete recovery from the depression of the peripheral blood values which may be assumed to have followed the bombing. Various significant differences between the two populations, however, were observed:

1. Erythrocyte count, hemoglobin concentration and hematocrit reading were slightly, but significantly, depressed for the subjects in Hiroshima.
2. Although the total leukocyte count was the same in the two cities, in Hiroshima there were a slight relative depression of lymphocytes and a slight elevation of eosinophils.
3. Plasma protein values were possibly slightly higher in Hiroshima.
4. There was significantly greater variability in the observations made in Hiroshima than in those made in Kure.

These differences cannot be attributed to a differential response on the part of any particular age or sex group.

Epilated persons who experienced associated flash burns or trauma showed mean erythrocyte values which were higher, if anything, than the values for those who did not suffer such associated injury, from which it is inferred that the greater frequency of these injuries in Hiroshima than in Kure does not account for the hematologic differences between the groups.

Those individuals who by any number of criteria absorbed greater amounts of radiation tended to show the most pronounced depression in erythrocyte and lymphocyte counts and the greatest elevation in eosinophil counts.

It is felt that in view of the great medical and civil disruption which ensued in Hiroshima, caution must be exercised in attributing the slight recorded differences to the atomic bombing, although it seems possible that irradiation was, to some extent, responsible.

One graph; 12 tables.

1950

y to  
g of  
ts of

ively  
scalp  
dom;

nutri-  
ity of  
hima.  
Kure,

brief  
blood  
deter-  
ential  
tocrit  
umber  
pared  
popula-  
tween  
d epi-

or the  
m the  
ay be  
signifi-  
how-

ration  
cantly,

e same  
nt rela-  
vation

lightly

in the  
ade in

differ-  
or sex

d flash  
s which  
r those  
which  
ese in-  
account  
ps.

criteria  
o show  
rte and  
eosino-

nd civil  
caution  
ecorded  
t seems  
nt, re-